THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

OCTOBER, 1927

ORIGINAL ARTICLES.

GYNECOLOGIC FOCI IN RELATION TO SCLERITIS AND EPISCLERITIS AND OTHER OCULAR INFECTIONS.

By L. Mary Moench, M.D.

(From the Division of Medicine, Mayo Clinic, Rochester, Minn.)

The routine eradication of foci of infection in cases of certain ocular diseases has been approved by most ophthalmologists. The responsibility for detecting such foci, however, usually falls on the internist. It is my purpose here to call the attention of the internist to certain mild infections of pelvic structures, particularly of the cervix uteri, often negligible from a local standpoint, which seem to act as foci of infection in certain cases of scleritis and episcleritis especially, and in other inflammatory conditions of the eye occasionally.

The theory relating diseases of the eye to distant foci of infection has been clearly reviewed by de Schweinitz who says, "Bacteria may find favorable opportunities for growth, multiplication and entrance into the lymph systems . . . subsequently they may locate in certain tissues, for instance ocular tissue, either because they have developed a specific affinity for these parts and find conditions favorable for their growth, or because the resistance of these parts is reduced by some other agency and thereby favors the localization of the germ." The relationship between iritis and tonsillar and dental infection has been long recognized by ophthalmologists and bacteriologists. Attention has been called to the pelvic foci more recently. Zentmayer and others have presented cases inditing the prostate as a remote focus in ocular inflammation. Benedict, von Lackum and Nickel have testified to the close relationship between pelvic infection, including that of the cervix uteri, and inflammation of the eye. They emphasize the interesting fact that "Infections

which become active, produce local abscesses and wide destruction of tissue rarely cause metastatic diseases of the eye. On the contrary, a focus of infection that shows little or no external evidence of disease not infrequently harbors organisms that give rise to serious diseases of the eye." It is this statement pertaining to the importance of apparently minor foci which is of special interest.

The time relationship between exacerbation of ocular disease and the menstrual period had been often observed by Benedict, who in 1924 reported the case referred to here. This patient reported in 1921 because of an extensive scleritis and episcleritis from which she had been suffering for seven months. In this case examination of the teeth did not reveal periapical infection and the tonsils had been removed elsewhere. The patient insisted that at each menstrual period the eyes invariably became more inflamed. Pelvic examination, however, did not disclose any lesion although there was a slight mucopurulent discharge from the cervical canal. Cultures of this discharge were positive for a slightly hemolyzing streptococcus. A vaccine made from this culture was administered in a dose that would now be regarded as unduly large. Within six or eight hours there occurred a general reaction with fever (101°) and a marked inflammatory reaction in the affected eye. This, however subsided within twenty-four hours and several days later resolution of the ocular inflammation was observed. Subsequent inoculations at weekly intervals did not produce any reaction either focal or local, but within four weeks the episcleritis had entirely subsided and the cure was permanent.

As a result of this striking case I have collaborated further with Dr. Benedict in studying the relationship between pelvic foci and certain infections of the eye in women. Routine pelvic examinations with culture from the cervix have been made for nearly six years in all types of ocular inflammatory lesions, especially scleritis and episcleritis. An attempt has been made to correlate these lesions with pelvic inflammation in both incidence and extent. In a certain proportion of women with ocular inflammation only mild endocervicitis of little clinical or local significance could be demonstrated, whereas in others rather extensive pelvic inflammation was present. There does not appear to be any parallel between the severity of the ocular symptoms and that of the pelvic infection, but the clearing up of the foci in the cervix has been associated in many cases with a striking subsidence of ocular symptoms.

The bacteria predominating in cases of ocular infection is often denoted by the character of the cervical discharge. In a study of the cervical flora of 82 miscellaneous cases of leucorrhea, published in 1924,[4] it was noted that purulent or seropurulent types of discharge were characterized by large numbers of streptococci, both aërobic and anaërobic. The mucoid leucorrheas, on the other hand, were productive of relatively few streptococci, but contained a higher

percentage of Gram-positive bacilli, colon bacilli and other members of the vaginal, vulvar and intestinal flora. This observation was previously made by Curtis.

Treatment. Whenever there is a discharge, especially of purulent or seropurulent character, even without other demonstrable signs of endocervicitis, the cervix is considered a probable focus of metastatic disease. Local treatment is accordingly instituted and an autogenous streptococcus vaccine administered. How much of the therapeutic effect of the vaccine is due to a nonspecific bacterial protein reaction is not to be considered in this report. In the majority of cases so treated, however, when other foci have not been demonstrable, the ocular inflammation has subsided and has remained in abeyance for from one to five years or has entirely disappeared. In many of these cases animal inoculation performed by Nickel has produced infection of the conjunctiva and iris in rabbits. It has, furthermore, been Benedict's experience that such autogenous vaccines are more satisfactory in every way than stock vaccines. The inoculations are given in doses sufficient to produce slight local or focal reaction only, at weekly intervals in series of ten to twelve.

In considering pelvic foci it is, of course, important to detect and treat the grosser pelvic infections. Careful inquiry as to previous salpingitis should be made, and in all cases of leucorrhea search should be made for residual tubal infection, or persisting low-grade pelvic cellulitis.

If definite laceration or long-standing endocervicitis has resulted in hypertrophy, erosion, or cysts of the cervix, a Sturmdorf operation with coning out of the cervical mucosa and glands is indicated. As regards surgical cautery, which may be satisfactory for local infections if the cervix is not implicated as a focus, it should be borne in mind that this procedure may result in the sealing off of the racemose glands in the deeper cervical tissues and, by interfering with drainage, throw more inflammatory products into the blood stream. This would tend to aggravate the distant metastatic disease and so defeat the purpose of the treatment (as probably illustrated by Case X). Moreover, there is danger of a violent focal reaction in the eye as a result of absorption of the protein of destroyed tissue from radical cautery of the cervix.

In recent and mild endocervicitis, however, when the canal is dilated and the tissues are spongy the linear cautery of the walls of the canal, lightly applied and spaced to avoid stricture, is often more effective and economical of time than antiseptics and dyes locally applied. In the treatment of simple erosions the linear cautery is especially efficacious. In older women where the cervix is extensively involved high amputation may be warranted. In selected cases of chronic tubal infection or high and extensive endocervicitis in the presence of a disease of the eye rapidly compromising the

vision, abdominal hysterectomy and salpingectomy may be considered. In all cases, however, a persistent attempt should be made to secure a vaccine before treatment, either medical or surgical, is instituted. In all cases, treatment should be as conservative as is consistent with eradication of the focus and the importance of the ocular condition.

Technique of Culture. For the taking of the culture the following simple technique previously described is employed. A sterile speculum is inserted and the mucus or pus removed from the external os. A sterile swab is then inserted into the cervical canal or, if possible, material is obtained from a punctured cervical cyst. This is inoculated into a tube of dextrose brain broth, a culture medium offering both aërobic and partial-tension conditions. If the growth, after eighteen or twenty-four hours, is free from contaminating organisms it is used for the vaccine. Gram-positive bacilli in any number render cultures unfit for vaccine purposes, whereas Gram-negative bacilli in small numbers are disregarded.

Report of Cases. CASE I.—A married woman, aged thirty-six years, came to the Mayo Clinic in March, 1924, because of inflammation in the right eye, the onset of which occurred during the latter part of November, 1923. There was slight redness and elevation at the outer margin of the cornea on the temporal side. Treatment was instituted but the lesion did not heal, instead it spread downward. About the middle of the following January an ulcer developed in the upper nasal quadrant of the cornea. Unproductive search was made for foci of infection by the usual methods as well as by Roentgen rays of the teeth and sinuses. The tonsils had been removed in 1920.

Examination at the Clinic revealed moderate injection of the palpebral conjunctiva. The ocular conjunctiva was injected all the way around the limbus. The sclera was deeply purple and the injection of the conjunctiva over this area was slightly greater than elsewhere. The limbus was slightly overgrown and the cornea hazy and infiltrated. Under the microscope the infiltration of the cornea was seen to be very deep. The patient was referred for general examination with special reference to the possibility of tuberculosis and focal infection. A roentgenogram of the chest and blood Wassermann tests were negative. The tonsils had been cleanly removed, and no periapical infection was found. A slight cervical discharge was revealed and a vaccine was made from this. During the initial series of inoculations with the vaccine the redness and elevation about the temporal side of the limbus disappeared.

April 19 a note was made that the eye was much improved. A faint fringe showed on the temporal side of the cornea. The patient did not complain of photophobia or sensitiveness, and nodules were not present. She was dismissed and the vaccine given by her local physician. August 5th she returned for further treatment. The eye had been clear of redness most of the time since her dismissal. The conjunctiva was not injected; the cornea had irregular nebulas beginning at 9 o'clock and extending below the anterior pole. She was referred to the gynecologic section for further cervical cultures for vaccine to be administered by her local physician.

This patient had not been heard from for about a year but in reply to a letter of inquiry dated January 1, 1927, she stated that the

eye had entirely cleared and that the infection had not recurred since her last visit, although there had been an intervening pregnancy.

CASE II.—A married woman, aged fifty-nine years, had had symptoms of ocular disturbance since October, 1923, when there was a subconjunctival hemorrhage in the left eye accompanied by irritation which had cleared gradually. In August, 1924, she noticed after a drive that the eye again became much irritated. The condition did not subside.

Examination revealed slight epibulbar congestion more marked on the nasal side. On the conjunctival limbus at 4 o'clock there was a small nodule beyond which the sclera was thin and discolored. In the left eye, there was slight conjunctival injection which disappeared under pressure, exposing a slight discoloration of the sclera and moderate thinning of this tissue about the cornea about 5 mm. in width. The eyes were otherwise normal. The tonsils were slightly enlarged but pus could not be expressed. A culture made from a mucopurulent cervical discharge produced hemolytic streptococci. The vaccine made from this growth was given weekly from June to July 16, 1925, during which time there was a gradual decrease in the scleral injection without exacerbation. A letter from the patient in January, 1927, stated that the trouble had subsided promptly. After the first series of treatments her attending physician had told her that there was no need to resume the use of the vaccine.

CASE III.—An unmarried woman, aged forty years, reported to the Mayo Clinic in August, 1926, complaining of inflammation of the right eye. This began in January, 1925, when she first noticed a network of bloodvessels in the temporal side of the ocular conjunctiva. The inflammation had been regarded as of tuberculous etiology and was so treated. The condition had varied, but it had increased rather than improved. A specialist in the East, consulted at the beginning of the trouble, had advised tonsillectomy and later several teeth had been extracted, but the inflammation had progressed in spite of these procedures. The general health had always been satisfactory.

On examination, marked injection of the palpebral and ocular conjunctiva was observed. The cornea contained white opacities, one at the limbus at 9 o'clock and the other just inside of it. In the right eye appeared a thickening of the episcleral tissues with nodules of translucent material surrounded by areas of vascularization. For the last two years, there had been a definite exacerbation of symptoms at the menstrual periods, and accordingly a general examination was made, including investigation for pelvic foci. Questioning revealed a history of possible gonorrheal infection five years previously and there was deep injection of the anterior lip of the cervix. There was tenderness in both adnexa indicative of low-grade salpingitis. All other foci had been removed. The blood Wassermann test and roentgenogram of the chest were negative. In view of the possible pelvic relation, and the presence of a fibromyoma with increasing menorrhagia, total adbominal hysterectomy seemed justified. Prior to this surgical procedure, however, a vaccine was made from the cervical discharge. August 27, total abdominal hysterectomy and bilateral salpingectomy were performed.

On examination September 21st, the episcleritis was much less intense than before operation and the clouded area in the cornea was gradually becoming thinner and withdrawing toward the limbus. By September 30, the inflammation was considerably reduced and vaccine was administered. The inflammation increased slightly as a result, but it subsided rapidly and there was no further reaction. The patient was referred to her home physician for further vaccine administration.

January 12, 1927, this patient wrote that there had been a gradual improvement since the operation. From a close examination she reports: "There are still fine red veins to be seen and on the right of the iris there is a faint spot yet. I feel, if it continues to improve as it has, in six months my eye will be normal again."

CASE IV.—An unmarried woman, aged thirty-one years, reported at the Mayo Clinic in December, 1925, because of inflammation in the right eye. Examination of the eye revealed early episcleritis. The onset had been coincident with the menstrual period, and throughout the subsequent course of the infection the eye had become more injected prior to and during menstruation.

In 1921, there had been some question of salpingitis but the condition had subsided under medical treatment. Inflammation in the tubes was not demonstrable at the examination in December, 1925. At this time examination of the pelvis revealed evidence only of endocervitis with injection of the cervix and a mucopurulent discharge. The cervical canal was lightly cauterized, following which soda douches and a streptococcus vaccine made from the discharge were given at weekly intervals until the inflammation subsided. In March, 1926, the tonsils were removed because of infection and it was found that the condition of the eye was normal. The patient reported in February, 1927, that the ocular infection had not returned.

CASE V.—A married woman, aged fifty-three years, came to the Mayo Clinic in June, 1926, complaining of inflammation of both eyes which had begun eighteen or twenty years before. During the last two years she had been troubled also with stiff joints. Examination of the eyes revealed some blepharitis and circumcorneal injection in both. The condition was considered old episcleritis with sclerosing keratitis, acute in the right eye.

Examination for foci of infection was negative. A roentgenogram of the teeth did not reveal periapical infection. The tonsils were small and apparently normal. A blood Wassermann test and investigation for intestinal parasites and the bacillus of tuberculosis were negative. A roentgenogram of the right foot revealed hypertrophic arthritis. Examination of the pelvis revealed a slight purulent discharge from the canal, from which a culture was made. Infection of the conjunctiva and iritis developed in the animals inoculated from this culture and a vaccine was made for the patient from this strain. She was advised to use hot soda douches and mercurochrome suppositories and was referred to her home physician for further administration of vaccine and treatment of the cervix. Eight months later she sent word that the acute condition had subsided and that there was redness only following unusual eye strain.

CASE VI.—A married woman, aged sixty-one years, was referred to the Mayo Clinic in December, 1925, by an oculist who had treated her for eight months for inflammation of the eyes. This had begun in March, when there had been frequent attacks of severe pain accompanied by marked injection, nodules on the eyeball and dimness of vision.

On examination, the conjunctiva was found injected, particularly above the cornea, the sclera was thickened and bluish around the upper and temporal sides, and there were small areas of sclerosing keratitis on the superior and temporal sides. General examination for foci seemed indicated. The tonsils had been removed previously. There was slight infection about one root tip and a slight amount of pyorrhea. Examination of the pelvis revealed nothing abnormal except laceration of the perineum. The cervix was small and not injected, but there was a discharge. Cervical streptococci

were used as a vaccine. Word was received in January, 1927, to the effect that the eye trouble had entirely subsided during the vaccine treatment.

CASE VII.—A married woman, aged forty-one years, registered at the Mayo Clinic in April, 1926, on account of redness and pain in the right eye. From March to about October, 1925, there had been a constant redness in the right eye without pain. In October the redness increased and a physician advised dental work. The pyorrhea was treated at this time and the injection of the eye promptly diminished. The improvement lasted until January, 1926, when the injection returned accompanied by pain and photophobia. More dental work gave partial relief of symptoms. The redness was marked at the border of the iris during February, and the latter part of March the redness again increased with pain and photophobia. These symptoms had persisted.

The examination revealed a marked purple circumcorneal injection and the cornea appeared hazy. There were three leukomas at its periphery and the iris was discolored. A general examination was made, with special reference to foci of infection. The data were essentially negative. The tonsils were graded "2" but pus was not expressed and they appeared innocent of infection. The laboratory tests, including a blood Wassermann test, were negative. Tonsillectomy was performed on April 12, 1926, without influencing the condition of the eyes. Examination of the pelvis revealed a slight thick mucoid discharge from the cervical canal. The cervix was not injected. Streptococci and Gram-negative bacilli were recovered from culture of the discharge and a vaccine was made. Three subcutaneous injections were given at weekly intervals. A local reaction occurred within twenty-four hours of each injection and lasted about three days, with moderate exacerbation of infection in the eye. In view of this reaction the amount of vaccine was reduced. In August there was still evidence of keratitis although the scleritis had subsided. A fresh cervical vaccine was made at this time. An enthusiastic letter from the patient on October 13th stated that the eye was steadily improving.

CASE VIII.—A married woman, aged nineteen years, registered at the Mayo Clinic in November, 1922, with the complaint of pain in the right eye for two months.

Examination of the right eye revealed slight injection of the palpebral conjunctiva. The vessels in the bulbar conjunctiva were larger than normal. At the upper portion, there was a deeper injection with a pinkish discoloration indicating involvement of the sclera. The tonsils were fibrous and chronic tonsillitis was diagnosed. Periapical infection about two teeth was revealed in a roentgenogram. Tonsillectomy and extraction of the infected teeth were carried out in November, 1922, and injections of milk were given.

There were moderate exacerbations and periods of remission until June, 1926, when the patient returned with a typical flare-up of the scleritis. There was a raised area of scleritis and a deep ciliary injection entirely surrounding the cornea. General examination revealed a mucopurulent leucorrheal discharge that she had had for several years, a heavy mucoid discharge from a lacerated cervix, retroversion of the fundus, and normal adnexa. The patient had noticed that the last period coincided with the severe exacerbation. She was given local treatments of slow, hot douches and tampons, and a new vaccine and when last seen the discharge had practically ceased. On September 2, 1926, when she was last seen, the eye was entirely clear.

The following cases illustrate inadequate treatment of the pelvic focus. There was temporary improvement following the original treatment but later recurrence during the menstrual periods.

CASE IX.—An unmarried woman, aged twenty-six years, came to the Clinic in August, 1925, because of redness in the right eye during the preceding fifteen months. The last two months there had been constant injection. Many physicians had been consulted but the only focus of infection discovered, the tonsils, had been removed six weeks before.

Examination of the eye showed the palpebral conjunctiva slightly injected and the bulbar conjunctiva considerably injected, especially in the fornix A diagnosis of episcleritis was made. The general physical examination revealed an area of periapical infection about one tooth and some evidence of a purulent discharge from the posterior cervical fornix, from which a vaccine was made. The history of this case indicated that the most severe attacks developed a few days prior to the menstrual period, lasted accutely for two days, and subsided following the period. The treatment with vaccine caused gradual improvement although the condition did not clear entirely. The cervix had not been treated and this focus has probably not been entirely eradicated. The patient has been advised to return for treatment of the latter.

CASE X.—A married woman, aged forty years, was first seen at the Clinic in May, 1925, because of blindness in the right eye. The eye had been operated on two years before, and she had been blind in this eye ever since. The nature of the operation is not known.

There was no complaint referable to the left eye and it was normal on examination. The right eye was enucleated. The general physical examination was negative at this time except for Roentgen ray evidence of a healed tuberculous process in the right apex and for deafness of the combined type.

In June, 1926, the patient returned complaining of pain and injection of the left eye for two months, and examination revealed scleritis with some overgrowth of the limbus and one root tip, which was extracted. There was evidence by Roentgen ray of thickening over the sacroiliac joint, probably due to arthritis. The cervix was extensively lacerated with a wide area of erosion and a fairly profuse mucopurulent discharge, from which streptococci were cultured and a vaccine made. Because of local reasons, as well as the possibility of some focal bearing on the inflammatory condition of the remaining eye, amputation of the cervix was recommended. However, a thorough surgical cauterization was performed instead. There was no exacerbation of the ocular infection. In fact, on the patient's dismissal from the Section on Ophthalmology the sclera appeared normal. However, subsequent letters from this patient indicate that the infection, although improved, is still active and there is often monthly exacerbation coinciding with the menstrual periods. It is probable that the pelvic focus was not eradicated by the cautery and the patient has been advised to return for amputation of the cervix.

The two following cases of uveitis are presented because of the improvement following more radical surgical treatment for deep-seated pelvic inflammation.

CASE XI.—A married woman, aged forty-four years, was referred to the Mayo Clinic by her physician because of chronic uveitis and cataract. Some blurring in the left eye had been noted for three years. Examination by her home physician had revealed two areas of periapical infection. These had been removed and tonsillectomy has been performed. The patient had received potassium iodid and five injections of milk.

Examination of the right eye revealed some deep opacities in the lens

over an area 6 mm. in diameter. This area was sharply outlined, and in the zone beyond, the opacities were rather few and small. There were a few small vacuoles, for the most part in the posterior cortex, and some large stringy, fine, floating opacities in the vitreous humor. Examination for tuberculosis and syphilis was negative. This included an examination of the spinal fluid and a Wassermann test. A definite history of pelvic infection was lacking, although there had been several abortions with slight fever following. Some leucorrhea had been noted. Examination of the pelvis revealed a lacerated cervix with several cysts and one large cyst. The latter was punctured and a purulent discharge obtained which was different in character from the mucoid discharge usually present in these cysts. About 2 drops of thin purulent material were obtained for culture. The growth consisted of streptococci and Gram-negative bacilli. In view of this condition and the progressing uveitis, a Sturmdorf operation was advised. In an attempt to amputate the cervix, it was found impossible to pass the cervical cysts. For their complete eradication it seemed best to remove the uterus, and therefore vaginal hysterectomy was performed. Convalescence from the operation was uneventful, and following recovery the autogenous vaccine was given. The patient was dismissed from the Clinic December 10, 1926, at which time her vision had markedly improved.

Case XII.—A married woman, aged thirty-eight years, reported at the Mayo Clinic in June, 1926, with the complaint of blindness in the left eye and rapidly failing vision in the right. Ten years before, she had begun to have pain in the left eye with gradual loss of vision. She had been totally blind in this eye for two years. The pain and diminished vision were always most noticeable during the menstrual periods. The vision in the right eye was good until May, 1925, when it gradually began to fail but there was practically no pain in this eye except during the menstrual periods.

Examination of the eyes revealed phthisis bulbæ in the left eye and extensive uveitis in the right. Light perception alone was retained. The general examination did not reveal evidence of tuberculosis. The blood Wassermann test was negative. Dental roentgenograms revealed two devitalized teeth without evidence of infection, and infection was not demonstrated in the tonsils although they had not been removed. The patient had borne one child and had noticed leucorrhea following parturition profuse enough to require a napkin. Pelvic examination revealed a profuse purulent discharge and the adnexa were somewhat thickened and tender. In view of this observation and the seriousness of her eye condition, radical pelvic operation was considered. This was strongly recommended by the ophthalmologists from the standpoint of the eye disease. Total abdominal hysterectomy, bilateral salpingectomy and oöphorectomy and appendectomy were accordingly performed. The pathologic examination confirmed the clinical diagnosis of salpingitis and oöphoritis. During the patient's convalescence the two devitalized teeth were extracted.

A letter from the husband six months later says that her vision has improved so that she is able to perform her usual household duties. "To my mind she has done wonderfully." Her nurse received a letter written in her own hand testifying to this improvement.

Conclusion. 1. The pelvic structures in women may be a focus of infection in certain ocular inflammations.

2. There is no demonstrable parallel between the extent of the pelvic inflammatory process and that of the ocular inflammation.

3. The infection is probably streptococcal rather than gonorrheal.

4. Treatment by autogenous vaccine from pelvic streptococci is efficacious in cases of ocular inflammation, especially scleritis and episcleritis.

5. The procedure chosen for eliminating the pelvic focus should be as conservative as is consistent with complete eradication of the focus and the importance of the ocular condition.

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DISPLACEMENT OF THE HEART IN PNEUMONIA IN CHILDREN.

By J. P. Crozer Griffith, M.D.,

PROFESSOR OF PEDIATRICS IN THE GRADUATE SCHOOL OF MEDICINE OF THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

In the attention which has been paid in recent years to the condition denominated "massive collapse of the lung, or massive atelectasis" it apparently has been considered that the diagnosis rested to a large extent, so far as physical signs and Roentgen ray findings were concerned, upon diminished expansion of the affected side, displacement of the heart to the affected side and a high stand of the diaphragm upon this side. In a previous publication in reporting a case of massive collapse in a newborn infant, I[1] pointed out that there was a possibility of pneumonia producing a very considerable displacement of the heart to the affected side; and that consequently such displacement, as shown by the Roentgen ray, could not be accepted as positive proof of the existence of collapse. It is true that in collapse the displacement is liable to be greater; but this is only a matter of degree, and it is perfectly possible in pneumonia for it to be very decided. It is a fact, too, that a careful study of the case, with the other symptoms and physical signs present, makes the diagnosis of collapse usually not difficult, and that there are distinct causes discoverable which are not operative in pneumonia. Here only is emphasized that displacement of the heart in pneumonia may, and frequently does, occur.

The truth of this had been previously recognized by Hofbauer[2] and others as applying to adults, while St. Engel[3] refers to the high stand of the diaphragm which may occur in children with a pneumonic consolidation of the right lower lobe. The only detailed observations, however, which I have been able to discover are those respectively of Thoenes[4] and of Wallgren.[5] The former described 11 instances, all in young infants of from seventeen days to thirteen months of age, and all showing on Roentgen ray examination displacement of the heart to the affected side, or to that side chiefly involved when both lungs were diseased. Most of the cases were of bronchopneumonia occurring in decidedly marantic subjects, and all were severe, 8 of the 11 ending fatally. The work of Thoenes is valuable and very suggestive but open to some criticism. The age of the infants and the character and severity of the disease indicate the possibility that atelectasis had much to do in producing diminution in the size of the affected lung and, through consequent negative pressure, displacement of the heart to that side. In fact in all the 4 autopsies reported more or less atelectasis was observed. Further, in apparently only 1 case is it distinctly stated that later examinations showed the heart again occupying its normal position. A still more important criticism is that the Roentgen ray pictures are reproduced as outlines merely, not as the actual pictures themselves; and that even in these considerable distortion is evident, which might be claimed to make the displacement of the heart, to a certain extent at least, apparent only. Nevertheless, even admitting the force of these criticisms, Thoenes' paper is very convincing.

Wallgren made a similar report upon 8 cases, 5 of them being two years or more of age. In all the pneumonia was unilateral and apparently of the croupous type, and in none were there any clinical evidences of atelectasis. All the children were in previously good or very fair health and all recovered. In all of them later examination showed the heart again in the normal position. In making the Roentgen ray observations every possible care was taken to avoid distortion in the pictures. These, however, which like those of Thoenes are in outline only, do show this distortion in some cases, and are to a certain extent then open to criticism, although not at all to a degree to vitiate the author's conclusions.

For nearly two years I have been studying this subject in suitable cases occurring in the wards of the Children's Hospital of Philadelphia. In this I have had the valuable coöperation of Dr. Ralph Bromer, roentgenologist to the hospital, without whose aid and interest this work would have been impossible. To avoid all criticism, as far as this could be done, only such subjects were selected who appeared to have been in good general health before the development of pneumonia, and in whom the disease was acute, unilateral, and apparently of a croupous nature. This was done in order to exclude as far as possible the influence of any complicating

atelectasis in its action upon the position of the heart. It may be stated that in none of the children were there any evidences whatever of this disease. A Roentgen ray examination was made early in the course of the attack, and in those cases where cardiac displacement was found a second Roentgen ray picture was obtained before the child left the hospital. In some instances, through misunderstandings, this last examination was not carried out. In all, 40 cases of suspected pneumonia were examined, some of these being later discarded on account of the disease becoming bilateral, or because of the occurrence of empyema, or for other reasons. Of the 40 cases 16 exhibited displacement of the heart to the affected side. The second examination was intended to prove that the position of the heart was not a persistingly anomalous one which had existed before the occurrence of the pneumonia. Yet in view of the frequency with which displacement was found this second examination was clearly hardly required. Finally great care was taken as far as might be, to avoid distortion of the Roentgen ray pictures and all cases were excluded in which such distortion did occur to a degree which might vitiate conclusions. To make still more certain of the cardiac position, a 6-foot teleroentgenogram was obtained in addition to the ordinary picture showing the lungs and heart together. This teleroentgenogram naturally does not reveal the full extent of the pneumonic consolidation as well as do the nearer exposures. It should be said that before drawing conclusions careful measurements of the pictures were made and due allowance granted by Dr. Bromer for distortion due to any faulty position which is unavoidable in some instances. Further it should be added that the films were submitted by him to several members of the Philadelphia Roentgen Ray Society, the general agreement resulting that the pictures represented undoubted actual displacement of the heart.

There follow here a few illustrative cases:

Case Reports. CASE I.—Eleanor M., colored, aged eleven months, admitted to the hospital December 9, was said to have been ill for five days. Examination on admission revealed dullness on percussion and increased vocal resonance over the upper part of the right lung. The temperature fell by rapid lysis and was normal on December 14. The respirations were from 48 to 60 at first but lessened with the temperature. There were never any signs or symptoms of atelectasis. The first Roentgen ray, 6-foot film (Fig. 1), taken December 10 showed a dense shadow in the upper part of the right lung, typical of the appearance of croupous pneumonia, and a moderate displacement of the heart to the right. The second examination (Fig. 2) made on December 18 revealed the lung nearly clear and the heart returning to the normal position.

CASE II.—John D., white, aged nineteen months, admitted to the hospital December 18, was said to have had fever for two days. Examination gave diminished expansion, dullness on percussion, tubular breathing and some fine râles over the middle portion of the right lung. The temperature ranged from 102° to 105° but dropped quickly to normal on December 20.

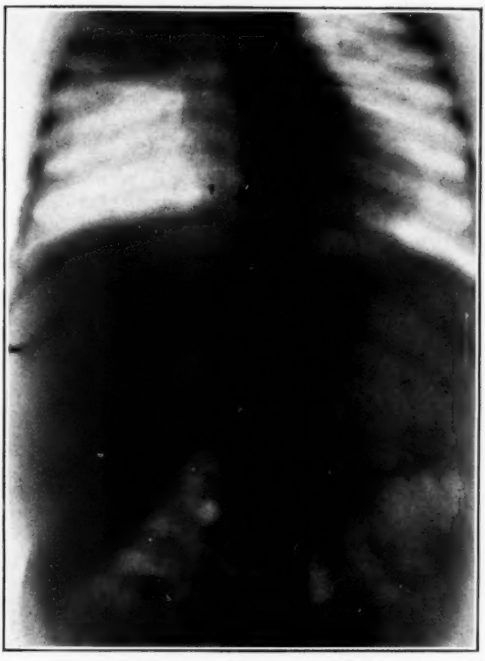

FIG. 1.—Case I. Eleanor M.: Consolidation of right lung. Moderate displacement of heart to the right. (6-foot film.)

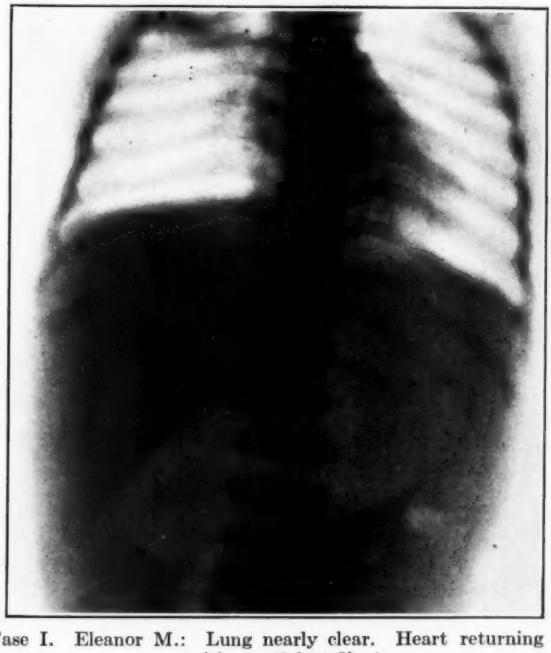

FIG. 2.—Case I. Eleanor M.: Lung nearly clear. Heart returning to normal position. (6-foot film.)

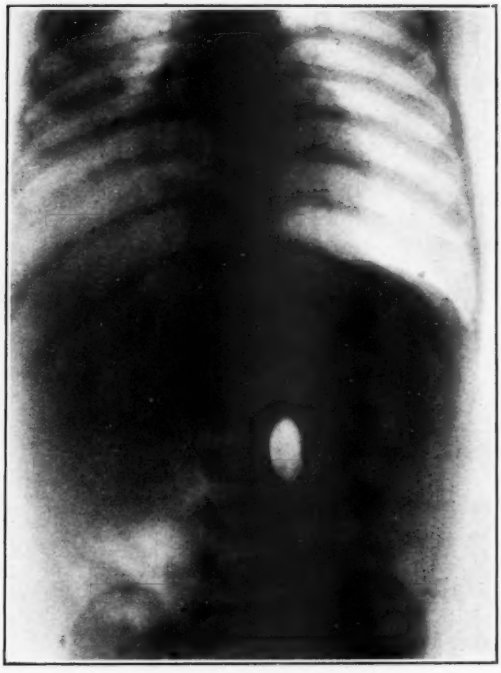

FIG. 3.—Case II. John D.: Partial consolidation of right lung. Displacement of heart to the right. (6-foot film.)

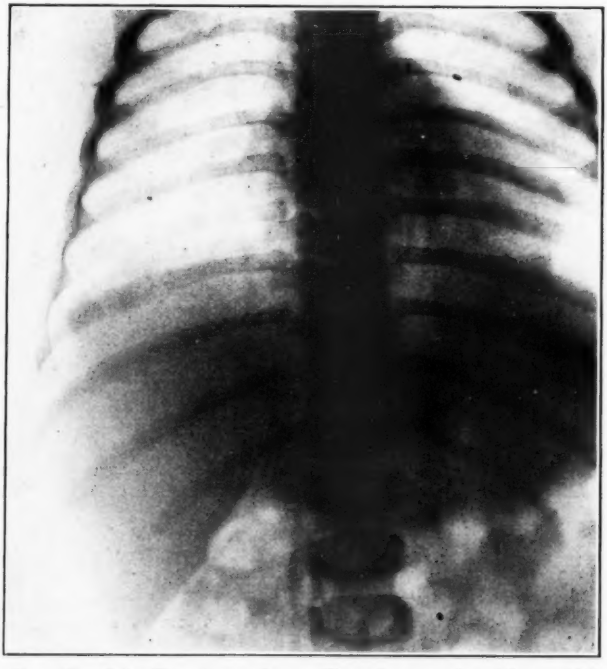

FIG. 4.—Case II. John D.: Lung clear. Heart in normal position. (6-foot film.)

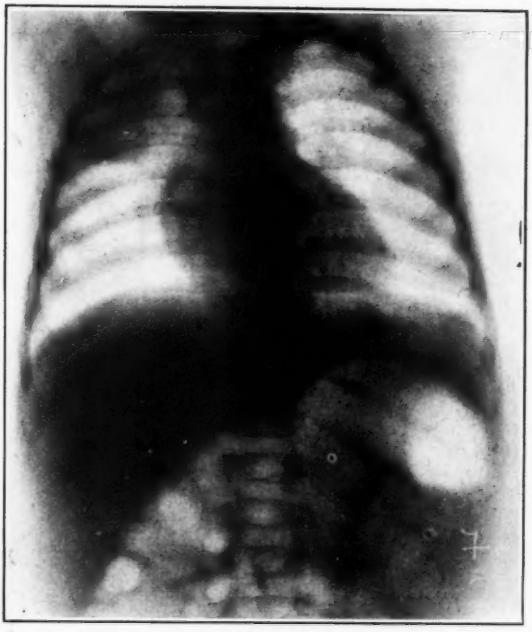

FIG. 5.—Case III. Alice U.: Delayed resolution in pneumonia. Heart still displaced to the right. (6-foot film.)

FIG. 6.—Case IV. Helen T.: Consolidation of left lung. Displacement of heart to the left.

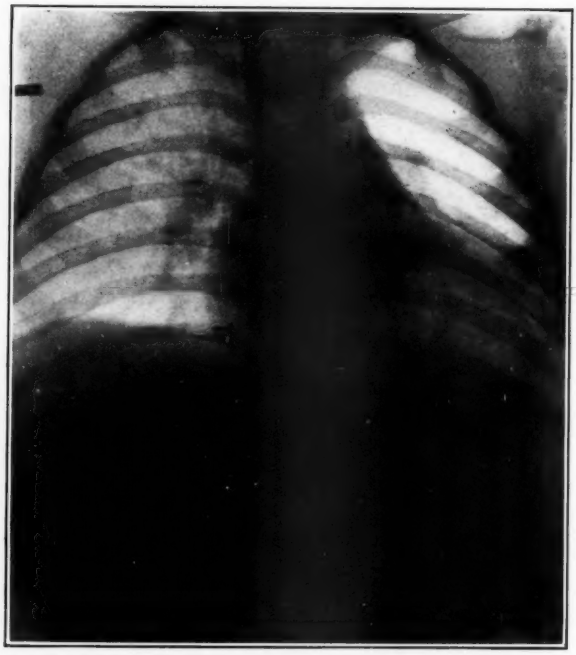

FIG. 7.—Case IV. Helen T.: Heart now in normal position.

There were never any symptoms or physical signs of atelectasis. On December 25 the child was quite convalescent although there were physical signs of delayed resolution.

The first Roentgen ray examination made December 19 revealed consolidation of the middle portion of the right lung, and a 6-foot film (Fig. 3) moderate displacement of the heart to the right. A second teleroentgenogram (Fig. 4) taken on January 4 showed the heart in the normal position.

CASE III.—Alice U., colored, aged six months, admitted to the hospital March 6, was said to have developed fever and rapid respiration on February 26, but the exact date of the onset of the disease was uncertain. Examination on admission discovered well-marked evidences of consolidation over the right apex in front and over the whole right side behind. The temperature fell slowly and by March 8 was normal and the general condition improved, although signs of delayed resolution were to be found. There were never any evidences of atelectasis. Roentgen ray examination on March 8 showed a dense shadow over the upper part of the right chest and slight displacement of the heart to the affected side. A second examination, 6-foot exposure, taken on March 15 (Fig. 5) exhibited the presence of delayed resolution but with a slight diminution in the density of the shadow. The heart was still displaced. No later Roentgen ray studies could be made in this case.

CASE IV.—Helen T., white, aged twenty-one months, admitted to the hospital December 22, was said to have had fever and cough for two days. Examination detected extensive dullness over the left lung with bronchial respiration and moist râles. There was no evidence of atelectasis. The temperature fell to normal on December 24. There was decidedly delayed resolution of the lung. Roentgen ray examination (Fig. 6) (not 6 foot) on December 26 showed a shadow over the entire lower part of the left side of the chest with definite displacement of the heart to the affected side. A second Roentgen ray picture (Fig. 7) on January 11, revealed decrease in the density of the consolidation and the heart now in the normal position.

The following 3 cases may be given with brevity as corroboration of the findings in those in which Roentgen ray pictures have been reproduced. Further multiplication of case histories and pictures seems unnecessary.

CASE V.—William C., colored, aged fifteen months, was admitted to the hospital January 6. There were typical symptoms of croupous pneumonia with sudden onset and consolidation of the upper part of the right lung posteriorly. The temperature fell promptly; there was no evidence of atelectasis. The Roentgen ray examination exhibited consolidation of the right lung and displacement of the heart to the right. The resolution of the lung and return of the heart to the normal position were delayed.

CASE VI.—Ruth W., colored, aged two years, admitted to the hospital January 13, had had cold and fever and rapid respiration for three days. Examination showed consolidation of the right lung with slight decrease of expansion, diminished breath sounds and fine râles with increased vocal resonance and prolonged respiration; there was no cyanosis. Roentgen ray examination revealed a dense shadow over the entire lower half of the right lung and a very decided displacement of the heart to the right.

CASE VII.—John P., white, aged sixteen months, admitted to the hospital January 30. This was a very typical case of wandering pneumonia confined to the right side. The heart was displaced to the affected side.

Comment. In view of the previous studies which have been made and of the confirmatory observations now reported, it would appear certain that in a very considerable number of cases of pneumonia there occurs a displacement of the heart to the affected side. Sometimes it is very decided; more often of moderate degree. The frequency of cardiac displacement is uncertain. Since we observed it 16 times in 40 cases examined, it clearly is of considerable frequency. Wallgren expressed a similar belief. As to whether it may occur frequently in adults no opinion can be given, inasmuch as it does not appear that there have been any detailed observations recorded.

The cardiac displacement is a temporary one only. The lung is sometimes clear before the heart has resumed the normal position. If there is delayed resolution the return of the heart is delayed as well. In at least two of my cases the heart returned to its place before the lung was entirely clear.

The cause of the displacement is open to discussion. Thoenes was inclined to attribute it to a complicating atelectasis, which caused a diminution in the size of the diseased lung and a consequent drawing of the heart to that side. The character of the disease in his cases, the early age, the severity of the attack, and the unfavorable outcome in most instances, make this explanation very possibly true, at least in part. Wallgren believes the cause was a compensatory dilatation in the healthy lung, which was obliged to do extra work on account of the interference with respiration in the pneumonic lung, through the infiltration in portions and the general diminution of elasticity. This extra expansion of the lung naturally encroaches upon the mediastinum and pushes the heart toward the pneumonic side. The disease in Wallgren's cases was of a different type from that in Thoenes' series; and in my own cases careful selection was made in order to include only those subjects who had previously been in good health, and in whom there was absolutely no clinical evidence of a complicating atelectasis during the course of the pneumonia. It would appear, therefore, far more probable that the distention of the healthy lung is the cause of the cardiac displacement. It is very possible, however, that the development of any atelectatic patches is a not infrequent aid in some instances in producing the displacement of the heart by diminishing the size of the diseased lung.

All the studies reported, my own and others, have been based upon film exposures. Fluoroscopic examinations might perhaps have been of advantage. Three such are reported by Wallgren and the observation made that no change in the degree of displacement of the heart occurred during respiration. Efforts were made both by Thoenes and Wallgren to correlate percussive and auscultatory signs, showing the position of the heart, with what was discovered on Roentgen ray exposure. The results were not very convincing;

and accordingly I have depended entirely upon Roentgen ray studies with teleroentgenograms for the purpose of determining accurately the position of the heart.

Conclusions. Of 40 cases diagnosed as pneumonia, 16 showed displacement of the heart to the affected side. A few of these are to be excluded in drawing conclusions on account of later developments. The reports of 7 of the cases are given in detail. The character of the disease in the cases examined indicated that the majority were instances of croupous pneumonia without discoverable evidences of atelectasis.

It may be concluded that the cardiac displacement is dependent at least primarily upon distention of the healthy lung.

These observations are confirmatory, for the most part, of those made by Thoenes and by Wallgren. They would seem to be of importance, first, because so little has been written regarding the subject, and nothing at all, so far as I have discovered, in journal literature in English; second, because the relative frequency with which the displacement occurred shows that the condition is probably not at all infrequent; and third because the matter has a distinct bearing upon the diagnosis of massive collapse of the lung.

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AMNESIA, EPILEPTIFORM CONVULSIVE SEIZURES AND HEMIPARESIS AS MANIFESTATIONS OF INSULIN SHOCK.

By W. Lindsay Miller, M.D.,

and

J. H. Trescher, M.D.,

Baltimore, Md.

Since the introduction of insulin therapy, there have been numerous reports of a variety of clinical manifestations of so-called "insulin shock," often, but not always, associated with hypoglycemia. Banting[1] and Sevringhaus[2] report an unaccountable anxiety restlessness and sweating, with a desire for food, muscular weakness in the extremities with slight tremor, tachycardia, dilatation of the pupils, and fall of temperature, and with the continued fall of the blood sugar, convulsions, coma and death. Sevringhaus[2]

mentions disorientation and amnesia in cases without convulsions, and these symptoms would seem to occur in reactions milder than those accompanied by convulsions and coma. In the 5 cases of disorientation and amnesia reported by Sevringhaus, disturbances of speech and sleepiness seemed to replace the usual premonitory symptoms of insulin overdosage and prevented the patient's asking for aid.

In a case recently observed in the Johns Hopkins Hospital, the patient not only exhibited the commoner symptoms of insulin shock with hypoglycemia, but also speech disturbances and amnesia, with tonic and clonic convulsions, and on one occasion, a transitory right hemiparesis was observed.

Case History. R. T., white, male, aged thirty years, was admitted to the private ward service of Dr. L. F. Barker on December 4, 1926. He complained of "peculiar attacks with fainting," in which he lost control of his hands, had muscular contractions, and then, as he expressed it, "passed out" completely. These "spells" first made their appearance in July, 1926.

With the exception of a history of tuberculosis in his father, a paternal aunt, and one sister, there was nothing of significance in the family history.

In the past history, the commoner childhood diseases and an uncomplicated scarlet fever were the only illnesses experienced before the sudden development of rather severe diabetic symptoms, first recognized in July, 1924. He was treated by diet and insulin and remained in good health, until the onset of the peculiar nervous symptoms of which he complained on admission to the hospital.

Present Illness. In July, 1926, while walking, he became dizzy, his gait became unsteady, and his general appearance was said to be that of a drunken man. He was taken to his home where he fell, had difficulty in speaking, showed drooping of the right shoulder, a tendency to lean toward the right, and complained of numbness in his hands, feet, legs and thighs. His physician reports that during this attack, his pupils were dilated, though they reacted normally to light, his knee kicks and ankle jerks were markedly exaggerated (almost to clonus). The right abdominal reflex was hypoactive and the left abolished. This attack is said to have lasted for more than an hour, and the next day the patient was unable to recall any incident associated with the attack.

During the following five months he suffered numerous similar attacks of varying severity; several of them were characterized by weakness of the legs, or uncontrollable activity of the arms, although he remained entirely conscious. During this time, he had also numerous attacks of visual disturbances in which he said that he "saw double," but it would seem, after close questioning, that he experienced merely a blurring of vision, which disappeared when he went into the fresh air.

The general physical and neurological examinations were entirely negative. The routine laboratory studies (including Wassermann reaction, basal metabolic rate, and spinal fluid tests) were negative, except that the fasting blood sugar was 0.165 per cent.

Upon arrival in Baltimore, the patient stated that he was supposed to be taking a 2000 calorie diet and that he gave himself 26 units of insulin (Lilly) thirty minutes before each meal. Upon checking up four days later, it was discovered that during these four days, he had maintained a diet of a lower caloric value than he had supposed and he had taken (we estimated)

between 90 and 100 units of insulin each day. During these four days, before entering the hospital, he had suffered several severe attacks of unconsciousness. On one occasion, the attack began at 4 P.M.; two other attacks started at about 9 P.M.

Upon admission to the hospital, he was placed on the diet of 2000 calories that had been prescribed for him, and he was given 25 units of insulin before each meal. On the second night after admission to the private ward, he was found apparently unconscious about 9.30 P.M. He was sitting in a chair with eyes closed and muscles flaccid. He was put to bed where he remained in a condition resembling profound alcoholic intoxication. About midnight he had intermittent attacks of generalized tonic and clonic convulsions which lasted about one hour. At 2 A.M. it was noted that there was marked weakness in the right arm and leg with flattening of the right side of the face; the abdominal reflexes were abolished, he showed a tendency to fall toward the right, and his pupils were dilated and did not react to light. A sample of blood collected during the early part of the attack revealed a sugar content of only 0.03 per cent. On the morning following the attack, the patient was fully conscious and quite rational, but he did not remember any incidents that occurred during the attack, or for a period of time preceding it.

He remained some seventeen days in the hospital in order that his diet and the amounts and distribution of dosage of insulin might be adjusted to his actual requirements. During this period he had several attacks characterized by transient amnesia, pallor, sweating and weakness. At the onset of each of these attacks he was given orange juice promptly and all symptoms quickly disappeared. On discharge, he had been on a diet of 2790 calories for six days and the amounts of insulin administered had been gradually reduced until on each of his last three days in the hospital he had received 20 units before breakfast, 10 units before dinner and a final 10 units before supper. There were no insulin reactions during this three-day period. On the second day before discharge, the blood sugar findings were as follows: Before breakfast, 0.197 per cent; one hour after breakfast, 0.262 per cent; one hour after lunch, 0.137 per cent; one hour after supper, 0.091 per cent; and at 10.45 P.M., 0.055 per cent. The condition was obviously still far from satisfactory, but the patient could not be persuaded to stay in the hospital for further adjustment of diet and insulin recommended.

Discussion of the Case.—While in the hospital, this patient manifested the commoner symptoms of insulin shock as listed by Banting and by Campbell and Macleod[3] and also certain more unusual symptoms (speech disturbance and amnesia) reported by Sevringhaus; in addition to these, he had generalized tonic and clonic convulsions and once bit his tongue in one of these convulsive seizures. During mild attacks, there was blurring of vision, and during a severe attack the pupils were dilated and there was loss of the light reflex. Other signs of central nervous system involvement were: (1) A right hemiparesis; (2) a tendency to fall to the right; (3) variability of the abdominal reflexes, and (4) marked exaggeration of the knee and ankle reflexes. The definite hemiparesis following convulsions was a complicating factor in the diagnosis of the reaction and might be listed as another manifestation of insulin shock.

It is interesting to note: (1) that this patient recovered from his

most severe attack without glucose therapy, and (2) that the administration of orange juice at the beginning of subsequent attacks immediately relieved all the symptoms. The normal emptying of the stomach when the patient was having no symptoms, as shown by roentgenological studies, and the prompt response to orange juice early in the attacks, ruled out the possibility that the reactions in this case were due to the retention of food in the stomach because of spasm or of organic obstruction.

Since the blood sugar early in the patient's most severe reaction was as low as 0.03 per cent, it was evident that a high grade of hypoglycemia accompanied the attack, but this of course does not necessarily mean that the symptoms of the attack were due directly to the hypoglycemia itself. As Macleod and others have emphasized, the possibility of other intermediate factors must be kept in mind. In an analysis of 24 cases, John[4] reports insulin reactions with blood sugar levels at the time of the reaction varying from 0.394 per cent to 0.035 per cent, the reactions occurring at any time within two hours, one reaction having occurred immediately after the injection of 15 units of insulin. John also found that, on one day, a patient with a low blood sugar might show no reaction after a large dose of insulin or after repeated small doses, whereas, on another day, the same patient would show a reaction to a small dose of insulin when the blood sugar was high. In an earlier article,[5] he reported a wide variation in the response of patients to the same dose of insulin upon different days.

Petty and Knode[6] have found that in diabetics with high blood sugar, the insulin shock came when the blood sugar was rapidly reduced to within normal limits, and Josephs[7] found that in non-diabetic children subject to attacks of convulsions and vomiting after relatively short fasting periods, the blood sugar concentration fell more rapidly and to a lower level than in normal children used as controls. However, Foshay[8] found that in dogs and humans insulin causes a much greater reduction of corpuscular sugar than of serum or whole blood sugar. Experimenting with dogs, he found that the insulin shock reactions occur when the corpuscular sugar is markedly decreased in comparison with the serum and whole blood sugar, which may be well above normal limits at the time of the reactions. The administration of glucose to an animal in shock relieved the symptoms but he found no increase in the sugar of the erythrocytes, though the sugar of the whole blood and serum was increased appreciably. Macela[9] of the Czech University at Prague, considers some impurity of insulin responsible for insulin shock, and he reports having obtained a purified insulin that lowers blood sugar extremely but does not cause convulsions.

From such reports, it would seem that insulin shock reactions are not altogether due to hypoglycemia, but require some other factor.

We have no record of the patient's reactions coming on after a change in the supply of insulin; the insulin used was produced by the same firm (Lilly). His available blood sugar during a very severe reaction was at a very low level, and no other abnormalities were detected. The oral administration of glucose (orange juice) immediately relieved the symptoms when given at the onset of an attack and consequently only one severe attack was observed.

It is obvious that the phenomena of insulin shock, though most common in association with hypoglycemia, may undoubtedly occur in the absence of hypoglycemia. Hence it is necessary to think of other alterations in the metabolism that might be induced by hypoglycemia at times, or by certain other conditions at other times, alterations, however, that in both instances can be abolished by administration of glucose.

There are many clinical observations that make it seem probable that insulin shock is particularly prone to occur in persons with unstable vegetative nervous systems, and many of the phenomena of insulin shock can be explained as disturbances in autonomic domains. Thus the sweating, the tremor, the pallor of the skin, the dilatation of the pupils, the changes in the pulse rate, the cramp-like pains in the abdomen—all are symptoms of disturbances of autonomic functions. Müller and Peterson[10] maintain that insulin shock depends upon an acute disturbance of the autonomic nervous system; they consider this disturbance as a predominance of sympathetic innervations in splanchnic domains, associated with a predominance of parasympathetic innervations in peripheral domains, just the opposite of what obtains in peptone shock. The explanation offered is not entirely convincing, but it must be admitted that the innervations within the vegetative nervous system are profoundly disturbed by the insulin shock.

Another region in which the common factor in insulin shock reactions may possibly be found is that of the physical chemistry of the blood and tissues. Benedict and Harrop[11] some time ago showed that insulin reduces the amount of inorganic phosphorus in the blood, and they as well as Briggs, Koechig, Doisy and Weber[12] have shown that it reduces the potassium of the blood also. Häusler and Heesch,[13] who have studied the reduction of phosphates and of potassium after insulin administration, think that they have proved that it is independent of dilution of the blood by fluids absorbed from the tissues. Nechkovitch[14] believes he has proved that, in experimental animals, the cause of insulin spasm is a disturbance of acid-base equilibrium with alteration of the pH in the nerve centers. Gabbe,[15] experimenting on frogs, which, in winter, are very susceptible to insulin intoxication, finds evidence of greatly increased reflex excitability of the muscles and nerves after insulin administration; he, therefore, assumes that, in addition to the hypoglycemia produced, some special disturbance of intermediate

metabolism is responsible for the convulsions. For other similar conjectures, the recent collective review of Houssay[16] (1925) may be consulted.

We, ourselves, have wondered whether in insulin shock the disturbance of intermediary metabolism might not be somewhat analogous to that now known to occur in tetany. In this malady, there appears to be: (1) instability of the acid-base equilibrium, and (2) a disturbance in the relative distribution of the electrolytes in the blood and tissue fluids (diminution of calcium ions with relative increase of monovalent cations); there would even seem to be somewhat different tetanies varying according as the derangement of the cation series varies. It would seem, we think, worth while to investigate carefully the distribution both of anions and cations in the blood during insulin shock, in view of the possibility that deviations from the normal might be detected. In this connection, it is interesting to find that Levai and Waldbauer,[17] in their discussion of gluco-augmentators and gluco-depressors, assert that large doses of insulin when injected together with parathyroid extract and calcium acetate solution into rabbits, will not give rise to convulsions despite the fact that marked hypoglycemia follows. If these observations can be confirmed, they would lend support to the tentative hypothesis we have entertained.

Summary. 1. A patient, diabetic for two and a half years, presented at times the ordinary symptoms of insulin shock, and at other times the more unusual symptoms of dysarthria and amnesia. During one especially severe reaction, in addition to these symptoms, convulsions and a definite hemiparesis were striking features.

2. With an increase of caloric intake and a reduction and better distribution of the insulin doses, noticeable reactions were avoided.

3. Prompt administration of orange juice quickly relieved the milder symptoms, the speech disturbance, and the amnesia. The effects of the administration of glucose upon convulsions and upon hemiparesis could not be tested.

4. Although the patient's most severe insulin reaction was accompanied by a marked hypoglycemia (0.03 per cent) a review of the literature reveals the fact that this is not an invariable accompaniment of such reactions. In a search for the mechanism of the reactions that characterize insulin shock the possibility of alterations in the mineral metabolism should be kept in mind.

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ENCEPHALOGRAPHY.*

By R. W. Waggoner, M.D.,
PHILADELPHIA.

This paper is presented as a brief review of the literature on encephalography and also as an analysis of encephalographic studies on 10 patients from the neurological service of the Philadelphia Orthopedic Hospital and Infirmary for Nervous Diseases. Some of the air injections were made by Drs. H. H. Hart and J. N. Petersen.

Encephalography is a term used to describe the injection of air into the spinal canal for the purpose of obtaining a roentgenographic record of the ventricles, cisternæ and subarachnoid spaces of the central nervous system. Dandy was first to use the ventricular method for the injection of air and noticing that the subarachnoid spaces sometimes showed on the Roentgen ray film as well as the ventricles, he decided to try spinal injection of air. He states in his original article that the danger in intraspinous injection is greater than in ventricular injection, but he describes 3 cases which could not have been accurately diagnosed by any other means. At about the same time and independently of each other, Wideroe and Bingel described similar methods for the spinal insufflation of air with the same purpose in view.

Later investigators are of the opinion that the procedure is not as dangerous as previously supposed, and it has been advocated by a number of men both in this country and abroad. I have been unable to find any authentic report as to the mortality in this method. Bingel, however, states that he had made 300 injections before his first death occurred and that this was due to the use of carbon dioxid which was absorbed too quickly and was followed by hemorrhage into the tumor.

Several methods have been used for the introduction of air into the spinal canal. One of the first was to remove a small amount

* Read before the Philadelphia Neurological Society, February 25, 1927.

of the spinal fluid and replace it by an equal quantity of air with the same syringe. This procedure was repeated until the desired amount of air had been introduced. The process, however, was slow and awkward and the patient usually had a rather severe reaction. Later a somewhat complicated arrangement of tubes and a pressure flask with a three-way stopcock for connection to the lumbar puncture needle was devised. After some experience it was found advisable to maintain a continuous check on the cerebrospinal fluid pressure by the use of a manometer in order to keep the pressure as nearly constant as possible. A method described by Liberson makes use of a needle large enough to carry a small cannula. The

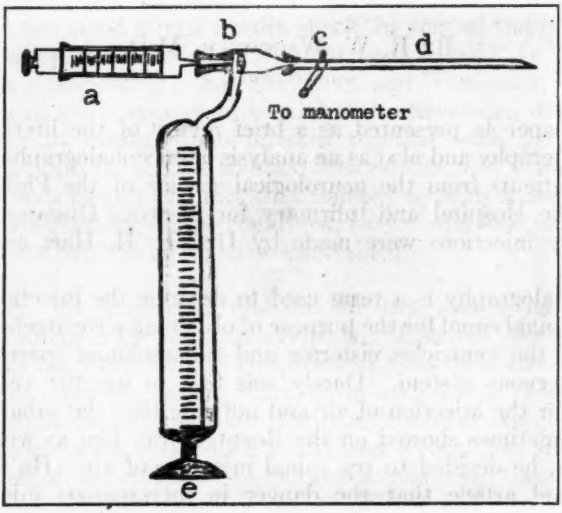

FIG. 1.—Reproduction of the apparatus used: *a*, a 10-cc. syringe; *b*, the three-way stopcock, by means of which a connection between the syringe and needle or between the syringe and cylinder may be established; *c*, a second three-way stopcock, which is an integral part of the lumbar puncture needle; *d*, the lumbar puncture needle; *e*, a graduated cylinder.

puncture is done and the needle and cannula are connected to a closed graduated cylinder in such a way as to make the cylinder, which contains air, an integral part of the cerebrospinal fluid system. The method involves the principle that when a liquid and air occupy a common container, the air will rise to the top. There are connections for a manometer, and for a syringe which is used to start the interchange of fluid and air. The cylinder is placed at a level which will cause the fluid to be displaced at the rate of about 5 cc. per minute.

The method I have used is one in which an ordinary Fleischer lumbar-puncture needle is connected to a manometer, a three-way

stopcock is placed in the needle and one arm is connected to a 10-cc. syringe and the other to a closed graduated cylinder. The fluid is withdrawn into the syringe and by changing the valve is injected into the cylinder from which the same or a slightly smaller quantity of air is removed and introduced slowly into the spinal canal. From 3 to 5 cc. of fluid are removed each time. It is important that the air be introduced into the spinal canal very slowly and steadily. If properly done, the patient will rarely complain of anything more than a moderate headache. Only 1 of the patients in my series complained of nausea or vomiting, although most authors seem to regard nausea and vomiting as a rather frequent complication. The patient receives a small dose of morphin and scopolamin shortly before the operation and if he complains of headache afterward, he is given another small dose of morphin. The puncture is done with the patient lying on his side, the pressure reading is taken and the patient is then placed in a sitting position, and the process of removal of fluid and injection of air is carried out; meanwhile a continuous check is kept on the spinal fluid pressure, which is maintained as nearly constant as possible. The head must not be too flexed on the chest during the injection of the air. The needle is then withdrawn and the Roentgen ray exposures are made with the patient still in the sitting position.

One anteroposterior film is taken with the film at occiput, the head tilted slightly forward and the Roentgen ray tube somewhat above the head in order to eliminate as much as possible the shadows of the nasal accessory sinuses. Two lateral views should then be taken one from each side. It is important that the head should not be inclined to either side when the exposure is made, otherwise there may result an apparent asymmetry of the ventricles and an increased amount of air in the subarachnoid spaces of the uppermost part. After injection of the air all the patient's movements must be very slow, otherwise he may develop nausea, vomiting or headache. The patient should remain quiet for at least twenty-four hours after the operation.

The indications for the use of encephalography are distinct, but it is a procedure that must not be used indiscriminately. In patients who have had a trauma of some kind to the skull, following which they manifest some nervous symptom complex that is alleged to have resulted from the injury, an encephalogram may be of value. It has been pointed out by O. Foerster and by Wartenburg that in practically all such cases definite organic deviations from the normal can be demonstrated. Thus at the site of the injury there may be found an increased collection of air in the subarachnoid spaces indicating a localized area of brain atrophy; also the ventricles are often dilated and drawn toward the side of injury.

Foerster has shown that the procedure is valuable in the differentiation of obstructive and communicating types of hydrocephalus.

In the obstructive or internal type practically no air will be found in the ventricular system and if the plates are sufficiently distinct the point of obstruction may even be demonstrated; this differentiation is important in determining the treatment and prognosis of the case. In true epilepsy of long standing, there is usually found a dilatation of the ventricle of the side on which the process started. Dilatation of the ventricles is a frequent finding in cases of encephalitis. In selected cases of brain tumor the procedure may be of great value in the localization of the lesion. It is comparable to ventriculography in results obtained and yet it is a much simpler procedure. Neurosurgeons often do not recognize the value of encephalography, since it is frequently of great aid in the diagnosis or differentiation of conditions which are primarily nonsurgical. Again it may often be used to determine the presence or absence of a surgical condition.

There are certain contraindications that should be borne in mind: thus encephalography should not usually be used in cases where there is high intracranial pressure because of the possibility of herniation of the medulla spinalis through the foramen magnum. For the same reason, it should rarely be used in cases of suspected posterior cranial fossa tumor. For obvious reasons it should not be used in cases of recent cerebral hemorrhage. It has been noted that attacks have become more frequent in epileptics after the use of encephalographly. however, some writers report good therapeutic results in simiar cases.

Case Reports. CASE I.—Male, aged eighteen years, with a clinical diagnosis of chronic encephalitis and with postencephalitic manifestations. Ninety cubic centimeters of air were injected with the removal of 100 cc. of cerebrospinal fluid. The patient had a severe headache which lasted for five to six hours; he also complained of dizziness, which persisted for four days. There was no nausea or vomiting. The films show an increased amount of air in the subarachnoid spaces especially in the region of the vertex, the ventricles are perhaps slightly dilated, suggesting brain atrophy. In the lateral view the cisterna magna and the shadow of the spinal cord can be demonstrated. The A-P view shows the butterfly figure formed by the lateral ventricles and the third ventricle.

CASE II.—Male, aged thirty-one years, with unilateral symptoms suggesting the presence of a cerebral cyst. One hundred and thirty cubic centimeters of fluid were removed and 119 cc. of air were injected. There is some asymmetry of the ventricles and an increased amount of air in the subarachnoid spaces of the left side. This finding is undoubtedly due to the tilting of the head and it will be seen that the films are well nigh worthless because of this fact. Nevertheless no evidence of a localized lesion was found and operation was not done. The patient later developed evidence of a diffuse process and now presents a typical multiple sclerosis syndrome.

CASE III.—Female, aged seven years, with a clinical diagnosis of epilepsy. An encephalogram was made under ether anesthesia. Thirty-five cubic centimeters of air were injected. The patient complained of some headache, but there was no nausea or vomiting, she was very quiet after the procedure. In this case there was not a sufficient amount of air injected.

FIG. 2.—Case I, practically normal. The butterfly figure of the ventricles is well shown in the *A–P* view and a clear outline of the ventricles, subarachnoid spaces, cerebellum and spinal cord is shown in the lateral view.

FIG. 3.—Case II. The *A–P* view illustrates the misleading results which may be obtained if the plate is made with the head tilted laterally. There is distortion of the ventricles and an increased amount of air in the subarachnoid spaces of the uppermost side. No evidence of a localized lesion can be seen; the patient later developed evidence of a diffuse process.

FIG. 4.—Case III. The *A–P* view demonstrates the presence of a porencephalic cyst of the right side; the wings of the butterfly figure are too irregular and too rounded. Not enough air was injected as is shown by the lateral view, although a marked irregularity and dilatation of the ventricles is demonstrated.

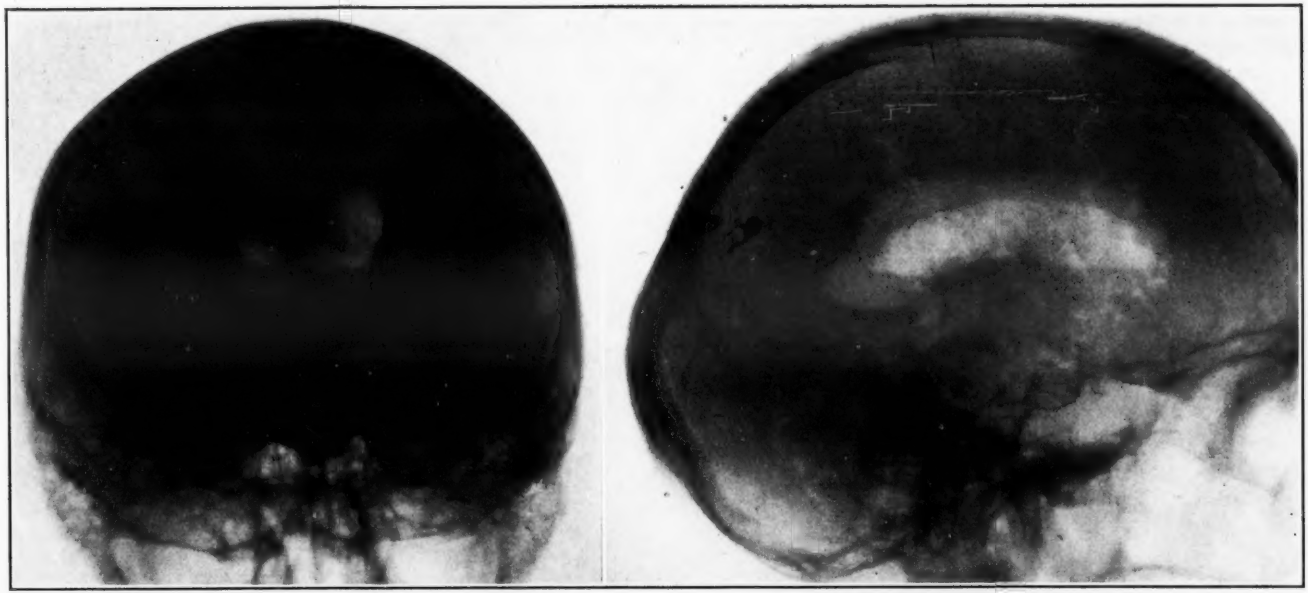

FIG. 5.—Case VII. There is dilatation of both ventricles, more marked on the left side, with definite rounding of the wings of the butterfly figure as shown in the *A–P* view. This abnormal dilatation of the ventricles is shown in the lateral view, which also demonstrates the presence of a lesion in the posterior cranial fossa.

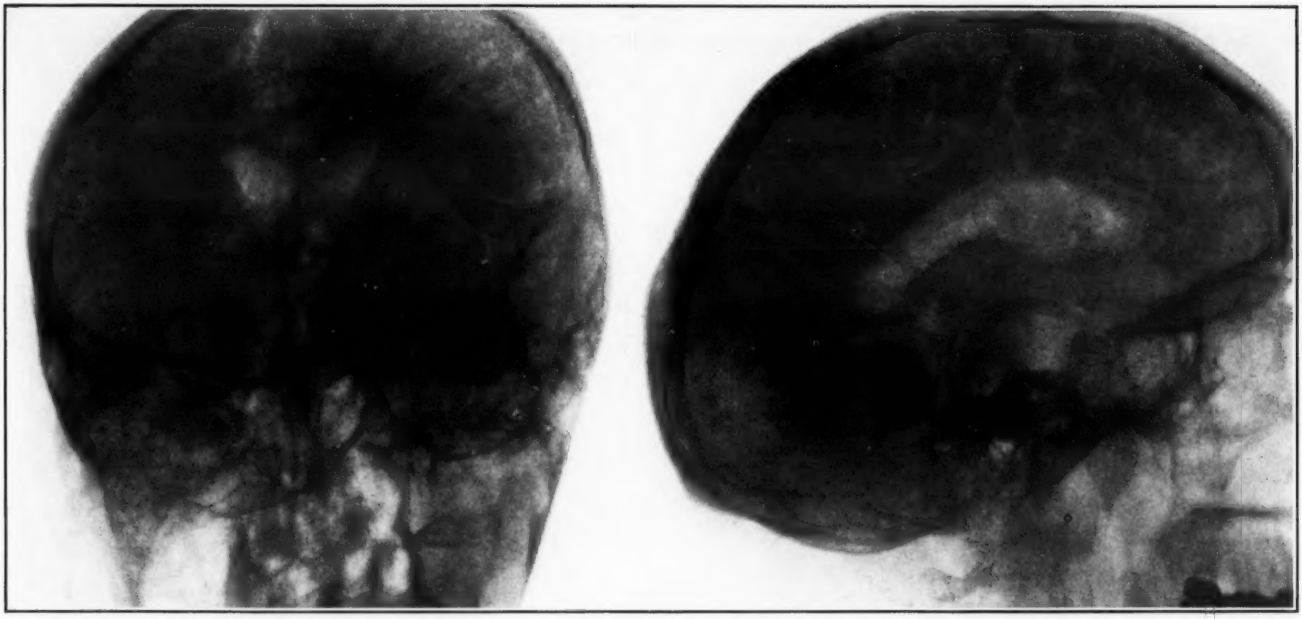

FIG. 6.—Case VIII. The *A–P* view demonstrates a marked dilatation of one ventricle; an increased amount of air in the subarachnoid spaces of the same side. It can also be seen that both ventricles are somewhat drawn to the affected side. The lateral view reveals a similar condition, but localizes the lesion in the temporal lobe. There is evidence of cortical atrophy over the frontal lobes. The basilar cisternæ are well shown in this plate.

FIG. 7.—Case IX. There is some dilatation and rounding of both horns, and there is also a well-defined collection of air at the vertex on the left side. The lateral plate demonstrates the anteroposterior position of the lesion. This lesion would undoubtedly have been overlooked in an encephalogram.

However, the Roentgen ray demonstrates the presence of a porencephalic cyst on the right side, and an increased amount of air in the subarachnoid spaces of the same side.

CASE IV.—Male, aged one and a half years, with a clinical diagnosis of imbecility. An encephalogram was made under ether anesthesia and 30 cc. of air injected. There were no bad after effects. There is a unilateral filling of the ventricles, the left being almost normally filled but showing some rounding of the ventricular horn. There is evidently some obstruction to the passage of air to the right lateral ventricle.

CASE V.—Male, aged four years, with a clinical diagnosis of imbecility. There is practically no air seen in the ventricles, while there is a comparatively large amount of air in the subarachnoid spaces. This is suggestive of an obstruction between the ventricular system and the subarachnoid spaces, which is probably the result of a meningitis which the child is said to have had at the age of three and a half months. No bad after effects were noted as the result of the air injection.

CASE VI.—Female, aged thirty-four years, with a clinical diagnosis of cerebellar neoplasm—after injection of 110 cc. of air, the patient had a rather severe headache for eight hours, but there were no other ill effects. The lateral ventricles are normal, there is an increased amount of air in the occipital and parietal regions especially of the right side. In the lateral view the cerebellum can be outlined, and there seems to be a definitely increased amount of air in the posterior cranial fossa, which would point to the presence of a lesion in that region.

CASE VII.—Male, aged forty-six years, with a clinical diagnosis of cerebellar ataxia. One hundred cubic centimeters of air were injected, there was no headache, nausea or vomiting. There is definite enlargement of the left lateral ventricle and with rounding of the horns of both lateral ventricles. There is an increased amount of air in the posterior cranial fossa indicating a pathological change in the region of the cerebellum.

CASE VIII.—Male, aged forty-six years, with a clinical diagnosis of subcortical hemorrhage of the left cerebrum involving the motoparietal area. After 90 cc. of air were injected, the patient complained of severe headache and nausea but there was no vomiting. According to the Roentgen ray there is dilatation of the right lateral ventricle and there is a large collection of air over the right motoparietal area. The encephalographic localization is correct for position in the hemisphere but on the wrong side of the brain according to the clinical data. I am inclined to accept the clinical diagnosis, and the possibility that the Roentgen ray plate was labeled incorrectly.

CASE IX.—Male, aged fifty-six years, with a clinical diagnosis of left frontal neoplasm. No severe reaction followed injection of 102 cc. of air. There is rounding of the ventricular horns of both sides. The left ventricle is slightly larger than the right and there is a small circumscribed collection of air at the left vertex just anterior to the position of the central fissure, which indicates the presence of a lesion in this area.

CASE X.—Female, aged fifty years, with evidence of a level lesion of the spinal cord by sensory examination and of a complete spinal cord block by Queckenstedt's test, preoperative diagnosis was spinal cord tumor. No disagreeable after effects followed injection of 50 cc. of air, although at

the time of air injection the patient complained of a drawing and bandlike sensation at the level of the lesion as indicated by the sensory examination. The ventricles contained a small amount of air, which indicated that the block was not complete. Air can be seen as high as the tenth dorsal vertebra which was approximately the level of the lesion as indicated by the sensory examination. At operation no cause for the spinal block could be demonstrated, although the cord appeared slightly smaller than usual.

Conclusions. 1. In a small group of selected cases, encephalography is a valuable aid in the diagnosis of intracerebral disease conditions; for instance, in the differentiation of the types of hydrocephalus, in determining the presence or absence of organic lesions of the brain following trauma, and in the localization of the lesion in selected cases of brain tumor.

2. If properly done, the procedure is without serious and in most cases without severe after effects.

3. The danger of its use has been overemphasized in the past.

4. Its value justifies its more general use but it is, perhaps, not without danger and should not be used indiscriminately.

5. In the one spinal cord case in which both tests were used the results agreed with those obtained by a Queckenstedt test.

Discussion. Dr. Fay: I believe that everyone will agree that this is the safest way of making a diagnosis in various obscure neurologic conditions. Dr. Waggoner's results are extremely interesting and I have had nothing worse than vomiting and headache produced by this procedure. I think some of these plates far superior to those obtained from the best ventriculograms. You can almost see the brain itself, not only the ventricular spaces but the cortical surface. I feel encephalography is going to replace ventriculography, except if the spinal pressure is increased, when it is unwise to remove the spinal fluid. In such cases the ventricle may be tapped, and after relief of pressure from above, air may be injected into the spinal canal, as well as the ventricle, thereby greatly lessening the danger. Dandy believes that in this way he can diagnose 99 per cent of brain tumors.

There is one point which I would make, which might help in the solution of this problem, and that is the importance of the simple gravity method of introducing air, in other words, measuring air introduced in terms of *pressure*, not volume. As you know, air at the 80 degrees of the operating room rises to 98 degrees in the body and consequently expands. Therefore if you put in 10 cc. of air for 10 cc. of fluid removed, you are going to have pressure. If you have a needle with a small connecting tube, and allow the fluid to go into the base of the bottle, it will replace the air in the cerebrospinal canal. I place another needle in the lumbar sac and that allows the fluid to run out, so that no air goes in until the fluid goes out sufficiently to prevent pressure. This will force the air until the manometer registers 10, and you should never allow the pressure to rise above 10.

I have had no untoward symptoms, aside from headache and vomiting. Rapid movement of the patients head will cause vomiting. I believe that this procedure is safe, and it is certainly not a difficult one. I think we shall use it more frequently for the purpose of diagnosis. I think Dr. Waggoner has made the first contribution in this line in Philadelphia, and it is worthy of being followed.

DR. GRANT: This whole question of encephalography and ventriculography as I see it, is this: you are introducing air into the brain with a fixed and definite purpose, that is, to find out, if you can, what the disorder within the skull may be and for the purpose of correcting that disorder. There is no question but that encephalography is easy and it is simple; but you still are faced with the fact that when you need ventriculograms most, it is not safe to use it, that is, in the face of intracranial pressure. The condition under which you can accomplish most for the patient following the injection of air into the cranial cavity is when a tumor is present, something which can be removed. A great majority of intracranial tumors produce intracranial pressure. I have no doubt that in cases of encephalitis, epilepsy and other cases of this type, you can obtain very good pictures of the cerebral cortex and of the ventricular horns being pulled to one side or the other.

It is curious that Dandy has given up encephalography, and that everybody who has attempted to use it in the removal of brain tumors, has given it up. When you are practising brain surgery, the chief condition is neoplasm. This gives you increased pressure, and therefore you are driven back to the use of ventriculograms in order to localize the lesion, and that, to my mind, is the great objective in the use of encephalography.

DR. WAGGONER: I have only two or three points to make. I appreciate Dr. Fay's description of his own method and his discussion of mine. However his method involves the use of two needles and makes necessary two lumbar punctures, which, of course, would cause the patient more discomfort. In making the injection, the volume of air introduced is always slightly smaller than that of the fluid removed, thus compensating for the expansion of the air. Since changes of pressure often cause disagreeable after effects, the pressure is maintained as nearly constant as possible by means of frequent manometer readings. I think Dr. Fay's method is similar to the one described by Bingel.

I wish also to thank Dr. Grant for the presentation of, his, the surgical viewpoint. In reply to his objection to the use of encephalography in cases with increased intracranial pressure, there is an article by Liberson in *The American Journal of Roentgenology* of March, 1926, which involves the use of an apparatus such as I have described by means of which he can maintain practically a constant pressure and thus it could be used in cases with increased intracranial pressure. Dr. Grant has discussed the procedure from a purely surgical point of view but he has not taken into consideration the use of a combined method of encephalography and ventriculography, which gives us the better results of an encephalogram without its supposed dangers in cases with increased intracranial pressure.

I think this procedure is as safe as an ordinary lumbar puncture. As previously stated, there is practically no mortality in its use. On the other hand, in ventriculography, there has been reported a mortality of from 3 to 9 per cent. Again, ventriculography requires the service of a skilled neurosurgeon, whereas with proper precautions encephalography can be done by anyone who can do an ordinary lumbar puncture. I believe the procedure has its place in the list of diagnostic methods and will come to be more frequently used.

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THE AMOUNT OF BLOOD FOR TRANSFUSION.

A Simple Method to Determine the Dose for Adults and Children.

By Harold W. Jones, M.D.,

PHILADELPHIA.

(From the Department of Medicine Jefferson Medical College Hospital.)

A satisfactory method to determine the dose of blood for transfusion does not exist, and too little attention is given to this question. An amount of 500 cc. is generally accepted as a standard dose, but many consider this amount just as satisfactory for a man 6 feet in height and weighing 200 pounds as for one of 100 pounds weight and only 5 feet in height. Even greater uncertainty seems to exist concerning the dose for infants and children. Often the amount transfused depends upon a guess which the operator makes. In certain disease conditions, different amounts of blood are indicated, yet it is not unusual that the same dose is used for all.

The dose must be influenced by the expectation of results. In acute hemorrhage an attempt should not be made to replace the total blood loss, but enough should be given to relieve the symptoms resulting from the deficient oxygen-carrying power of the patient's blood and to combat whatever degree of shock is present. In

simple chronic anemias, blood is administered to stimulate the bone marrow, to supply needed hemoglobin that oxygen interchange may be more nearly normal and to bring about an improved function in the various organs. In patients suffering from great fluid loss, transfused blood will supply fluid and nutrition and aid in regulating the acid-base equilibrium. Large amounts of blood are not essential to the accomplishment of these results. The technique of transfusion has been so simplified that it is performed as easily and with as little discomfort to the patient as any other method of intravenous medication. In the past, the administration of blood assumed the proportions of a major operation; the veins were exposed or arteries temporarily anastomosed. All these procedures were time-consuming and justified the use of large amounts of blood at infrequent intervals. Today transfusions may be given, if necessary, many times in a single day, using the same vein in each operation. Colwell [9] reported good results following the injection of 25 to 50 cc. of blood at short intervals. This dose is too small but emphasizes the fact that even such small amounts may be beneficial.

Standard Dose. As a result of experience in nearly 2000 transfusions, a dose of 400 cc. in primary anemia and simple chronic secondary anemia is recommended for an average adult of 150 pounds weight and 5 feet 8 inches in height. Most cases of secondary anemia[11] required but two to four transfusions of the amount mentioned to produce satisfactory results.

Acute Hemorrhage. In acute hemorrhage, the dose depends upon the extent of the blood loss. This loss is difficult to determine, because even as the hemorrhage is occurring, if the loss is not too sudden or too great, the tissue fluid begins to enter the bloodvessels and continues after the hemorrhage is stopped until the blood volume is normal and in some instances until the blood volume is greatly increased.[1] Keith[2] in using the vital-red method in soldiers with combined hemorrhage and shock, stated that in the most severe cases the blood volume was below 50 to 60 per cent of normal and that serious symptoms were not present until the blood volume was less than 75 per cent. Hemoglobin estimations made at the time of, or shortly after, a hemorrhage are often misleading and red blood cell counts are even less accurate. Because of these facts, it is suggested that enough blood be given to relieve the symptoms of the deficient oxygen-carrying power, that is, coma, stupor, rapid respiration (air hunger) and rapid pulse. However, as a result of experience with patients treated for acute hemorrhage, the following standards of dosage are recommended. If the hemoglobin following an acute hemorrhage is from 70 to 80 per cent, 500 cc. of blood may be used as a standard dose. If the hemoblobin is from 60 to 70 per cent, use 600 cc. If the hemoglobin is from 45 to 60 per cent, use 700 cc. If the hemoglobin is from 30 to 45 per cent, 800 cc. may be used as a standard. These standards are

based on the assumption that the hemoglobin is normal before the hemorrhage occurs.

Purpura Hemorrhagica and Acute Hemolytic Jaundice. In purpura hemorrhagica, if the patient is seen when a moderate secondary anemia is present, the standard dose is 400 cc. If there has been an acute blood loss of considerable degree, the standard for dosage should be the same as for acute hemorrhage. Transfusions should be given every three to five days but in the very acute cases it may be necessary to transfuse twice in one day.[3] The same dosage is recommended for use in acute hemolytic jaundice.

Splenic Anemia. In splenic anemia, the standard dose is 400 cc. unless the patient is seen at a time when the anemia is so severe that a larger dose is required to carry him past the danger point.

Hemophilia. In hemophilia, the standard dose is the same as that used in acute hemorrhage unless an anemia of a more or less chronic nature is present. The standard dose under such conditions is 400 cc.

Septicemia and Puerperal Sepsis. In puerperal sepsis plus anemia the first transfusion should be of 100 cc. If the blood is well borne, larger amounts may be used: 300 cc. at three- to five-day intervals. In other blood stream infections complicated by secondary anemia, small transfusions given at frequent intervals, that is, three to five days, have proved beneficial. The standard dose at the first transfusion should be 100 cc. If the blood is well borne then the standard may be raised to 300 cc. and the transfusions continued until the blood count is 70 to 80 per cent normal. In bacteremia occurring during the puerperium or under other conditions and not complicated by anemia; in burns and in pemphigus, 200 cc. of blood should first be withdrawn from the patient and then 300 cc. administered. This procedure may be repeated at three- to four-day intervals.

Addisonian Anemia. In Addison's anemia, 100 cc. are given at the first transfusion unless the condition of the patient is such that a larger amount is needed to carry him past the danger point.[4] Following this, blood is administered every three to five days, using 400 cc. as a standard dose.

Fluid Loss. In conditions characterized by great fluid loss such as cholera, severe dysentery, protracted and prolonged diarrhea and vomiting, the standard dose is 500 cc.

Nephritis and Arthritis. In chronic nephritis, plus secondary anemia, an initial transfusion of 100 cc. is best used. Following this, the amount may be increased to 400 cc. at five-day intervals. The same may be said of chronic arthritis plus secondary anemia.

In acute hemorrhage of the newborn, one must keep in mind the fact that the hemoglobin at birth is 100 to 104 per cent and steadily diminishes until the age of three weeks at which time it may be as low as 60 per cent.

Method of Dose Determination. A method of dosage based on body weight alone is not satisfactory. Haldane and Smith[5] state that the average blood volume is 4.8 per cent of the normal body weight and in an obese patient only 3.3 per cent. Boycott and Douglass[6] suggest that the figures for oxygen capacity and blood

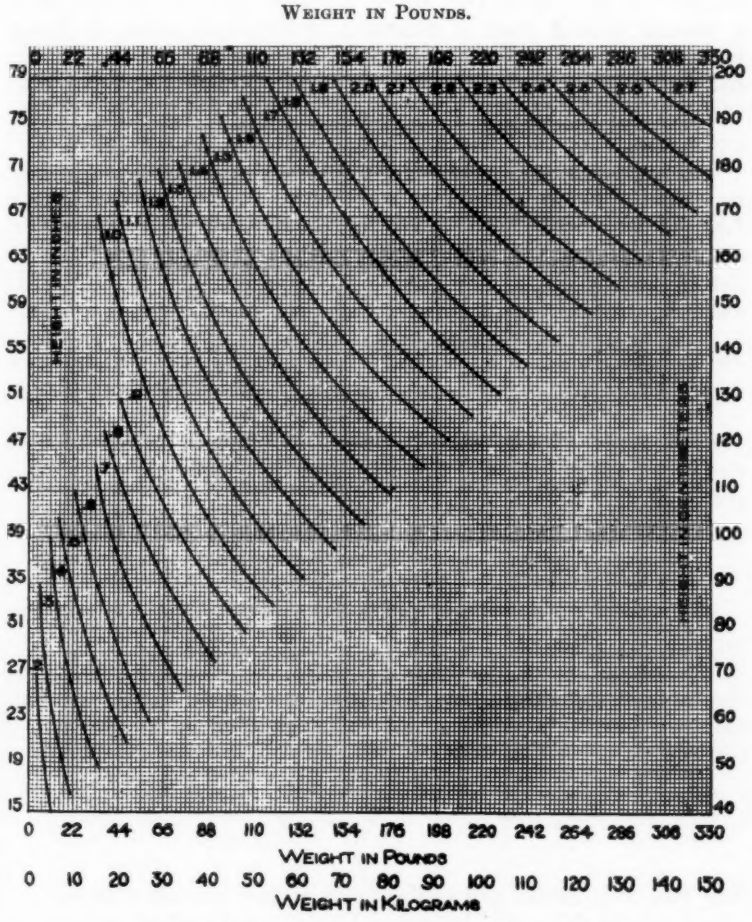

CHART.—Curve showing body surface in square meters.

volume per unit of body weight should not be used except when necessary, as a considerable rise in these values may mean that the subject has got rid of a lot of fat. T. Halbertsma[7] states that a rise of one million corpuscles corresponds with an amount of 15 cc. of blood per kilogram of body weight in children. Robertson,

Brown, and Simpson[8] use 15 cc. per pound body weight in children up to eighteen months.

The method herein offered for the determination of dosage depends not only on weight but also on the height of the patient. Using this method, those of short stature but very much overweight, receive no more blood than those of less weight but greater height. A tall person very much underweight can accommodate a greater volume than is indicated by the estimation of dosage from body weight alone. Using the formula of Du Bois[9] for the determination of square meter body surface, that is, Area (sq. cm.) equals Wt. $^{0.425}$ x Ht. $^{0.725}$ x 71.84, curves are plotted to include the body surface for all height and weight except the most unusual.

The average adult is said to be 5 feet 8 inches tall and 150 pounds in weight. The square meter body surface of the average man is 1.8. It has already been stated that the dose for the average adult is 400 cc. Using the following formula, the dose of blood may be determined for any square meter body surface, that is, any height and weight.

Standard dose : Standard surface area : : Unknown dose : Surface area recipient
400 : 1.8 : : x : .2

Example I: .2 is the surface area of an infant 20 inches in length and 8 pounds in weight. From the above formula the calculating is as follows:

$$1.8\,x = 80$$
$$x = 44 \text{ cc.}$$

Example II: Adult, 6 feet tall, weighing 200 pounds, with square meter body surface 2.15, has an acute hemorrhage which results in the reduction of the hemoglobin to 60 per cent. Following the table of standard dosage, the amount required for the average man with acute hemorrhage and a hemoglobin of 60 per cent is 600 cc:

$$600 : 1.8 : : x : 2.15$$
$$1.8\,x = 1290$$
$$x = 715 \text{ cc.}$$

The following tables will insure even greater certainty in dosage. The first table gives the height and weight and surface area for an individual from birth to nineteen years of age. If the child is greatly over weight, the dose may be calculated from the table giving the average weight of a child of the same age and height. These statements apply to adults as well and by using the table of standard weight for various height and age a more correct dose may be estimated.

STANDARD DOSE IN VARIOUS CONDITIONS FOR THE AVERAGE INDIVIDUAL.

Chronic secondary anemia, simple	400 cc.
Addison anemia	400 cc. (see text).
Acute hemorrhage:	
Hemoglobin 70 to 80 per cent	500 cc.
Hemoglobin 60 to 70 per cent	600 cc.
Hemoglobin 45 to 60 per cent	700 cc.
Hemoglobin 30 to 45 per cent	800 cc.
Purpura hemorrhagica	400 cc.
Purpura hemorrhagica with acute hemorrhage	Same as in acute hemorrhage.
Acute hemolytic jaundice	400 cc.
Acute hemolytic jaundice with acute hemorrhage	Same as in acute hemorrhage.
Splenic anemia	400 cc.
Hemophilia, acute	Same as in acute hemorrhage.
Hemophilia, chronic	400 cc.
Splenic anemia	400 cc.
Septicemia (see text).	
Puerperal sepsis plus secondary anemia	300 cc. (see text).
Bacteremia plus secondary anemia	300 cc. (see text).
Fluid Loss:	
1 Cholera	500 cc.
2 Dysentery.	
3 Starvation.	
4 Protracted vomiting.	
Chronic nephritis plus secondary anemia	400 cc. (see text).
Chronic arthritis plus secondary anemia	400 cc. (see text).
Pemphigus (see text).	
Burns (see text).	

MEAN WEIGHT VARIOUS HEIGHTS AND AGES.[12]

Height.		Ages.							
Feet.	Inches.	15–19.	20–24.	25–29.	30–34.	35–39.	40–44.	45–49.	50 or over.
5	0	113	119	124	127	129	132	134	135
	1	115	121	126	129	131	134	136	137
	2	118	124	128	131	133	136	138	139
	3	121	127	131	134	136	139	141	142
	4	124	131	134	137	140	142	144	145
	5	128	135	138	141	144	146	148	149
	6	132	139	142	145	148	150	152	153
	7	136	142	146	149	152	154	156	158
	8	140	146	150	154	156	158	161	163
	9	144	150	154	158	162	164	166	168
	10	148	154	158	163	167	169	171	173
	11	153	158	163	168	172	175	177	178
6	0	158	163	169	174	178	181	183	184
	1	163	168	175	180	184	187	190	191
	2	168	173	181	186	191	194	197	198
	3	173	178	187	192	197	201	204	205
	4	178	183	192	198	203	208	211	212
	5	183	188	197	203	209	214	217	219

STANDARD HEIGHT, WEIGHT AND BODY SURFACE FROM BIRTH TO EIGHTEEN YEARS.[13]

Age.	Height (inches).	Weight (pounds).	Body surface (square meters).
Birth	20	8	0.21
5 months	24	15	0.32
1 year	28½	21	0.35
2 years	32½	27	0.5
3 years	35	32	0.58
4 years	38	37	0.62
5 years	41	41	0.73
6 years	43½	45	0.79
7 years	45½	49	0.86
8 years	47½	54	0.91
9 years	49½	60	0.97
10 years	51½	66	1.04
11 years	53½	72	1.10
12 years	55	79	1.20
13 years	58	88	1.29
14 years	60	97	1.36
15 years	63	108	1.49
16 years	65	119	1.60
17 years	67	130	1.68
18 years	68	141	1.75

Surface area from curve chart shown in this article.

Conclusions. 1. The uncertainty in dosage for blood transfusion is discussed.

2. A standard amount of 400 cc. is set forth for the average man of 5 feet 8 inches height and 150 pounds weight.

3. The standard dose for the average man is given for use in various disease conditions.

4. Dosage of blood and blood volume estimations, based on weight alone, are inaccurate.

5. Curves are plotted from Du Bois' formula for body surface area, to include all heights and weights except the most unusual.

6. The formula for dose determination is:

Standard dose : Standard surface area :: Unknown dose : Recipient's surface area.

7. A table of normal weights from birth to sixty years of age is given.

8. If a patient is greatly overweight or underweight, the surface area may be calculated by using the normal weight for his height and age instead of his own weight.

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MULTIPLE SCLEROSIS.

With an Analysis of Eleven Cases Verified at Necropsy.

By Horace B. Conaway, M.D.,

and

Frederick C. Hill, M.D.,

Philadelphia.

(From the Neurologic Wards and the Laboratory of Neuropathology of the Philadelphia General Hospital.)

Many clinical and statistical studies have been made of multiple sclerosis, but most of the records available have not been complete, in that they did not extend up to the time of the patients' death. We have included in this report only those cases which have been followed throughout their entire course, and which have shown the lesions of multiple sclerosis at necropsy. This fact, together with the additional factor that in some of our cases the correct diagnosis was made only at necropsy, seems to give value to our data, even though they were obtained from a relatively small number of cases. We have also, however, in discussing the incidence of the disease, included for comparison an enumeration of all the cases diagnosed multiple sclerosis clinically in the Philadelphia General Hospital during the period of time which is covered by our cases with fatal outcome.

Multiple sclerosis has long been stated to be comparatively rare in the United States. Dana,[1] one of the first to call attention to this, found in 1902, that in New York City the incidence of multiple sclerosis among other organic nervous diseases was 3 per 1000. Taylor and Myer,[2] in reviewing 10,000 neurologic histories in Boston, in 1903, found less than 1 case per 1000. Collins[3] gave a rate of 5 per 1000 in New York, from a review of 9508 cases of organic nervous disease. On the other hand, Bramwell,[4] in 1903, found the incidence in Scotland and the North of England to be 12 per 1000. Jelliffe[5] reported that Saenger found 10 cases per 1000 in Hamburg, and Jolly, in Berlin, gave 8 per 1000. Oppenheim, in his textbook,[6] states that in his experience, multiple sclerosis is the most common of all the chronic organic diseases of the nervous system.

It will be noted that the American statistics given above are all some twenty years old. More recently (1922), Wechsler[7] computed from the records of the Mt. Sinai Hospital, the Montefiore Home and Vanderbilt Clinic in New York City that the incidence was 10 per 1000, showing that there had been a considerable increase since the older estimates were made. Whether this was due to

actual increase in the frequency of the disease, or to more accurate diagnosis, he was unable to say, but offered the following suggestions in favor of the latter explanation: (1) The Charcot triad is not considered as essential for a diagnosis now as it was formerly; (2) the importance of absent abdominal reflexes was not at that time as generally realized; (3) many of the older records were compiled before the Babinski reflex was known. Another explanation given is that some of the increase, at least, is due to the tremendous foreign population in New York City.

During the six years from 1921 to 1926, inclusive, 5469 patients were admitted to the neurologic wards of the Philadelphia General Hospital, and a diagnosis of multiple sclerosis was made clinically in 38 instances. This gives an incidence of 7 per 1000, a figure somewhat lower than those obtained by Wechsler, Saenger and Jolly, but higher than the older American statistics.

There were 1700 postmortem examinations of the central nervous system made in the Philadelphia General Hospital during this same six-year period. The lesions of multiple sclerosis were found in nine subjects. Two of these cases had been diagnosed clinically dystonia musculorum deformans and posterolateral sclerosis. There were 3 other cases in which a clinical diagnosis of disseminated sclerosis had been made, but which at necropsy showed cerebrospinal syphilis, arteriosclerosis and brain tumor, respectively. Two of the records which have been used in this study were on brains which were sent for examination from another hospital, and brought our series up to 11 cases.

Disseminated sclerosis is considerably more common in the male sex. In this series there were 6 males and 5 females. Wechsler[7] assembled the statistics of a large number of different observers, with a total of 1505 cases, and found the ratio 57 males to 43 females in the United States, and 58 to 42 in Europe.

The average age of onset of the disease in our autopsied cases was thirty-four years; the earliest occurrence of first symptoms was at twenty years and the latest at fifty-three years. The average age of onset determined by Wechsler was from twenty to forty years in 70 to 75 per cent of the cases. The shortest duration of the disease in our cases was two years, and the longest nineteen years, with an average of nine years. The average age at which death occurred was forty-one and a half years. The youngest subject died at twenty-six years, and the oldest at sixty-five years. Birley and Dudgeon,[8] taking the time from the onset of the first symptom to the time the patient came under observation, estimated the average duration at four years. This, of course, is too short, as the cases were not followed until death. The duration of multiple sclerosis in their case which gave the longest preclinical history was fourteen years. The shortest duration in their series was three weeks. Bramwell,[9] on the other hand, compiled his statistics only on

patients in whom the disease had terminated fatally, and found the duration to be from seven months to twenty-one years, with an average of seven and three-quarter years. This closely approaches our findings.

The etiology of multiple sclerosis is unknown, but there is some evidence that injuries or other exogenous agents may play a part in precipitating the disease. Two of our patients dated the onset of symptoms from a fall. In 1 case symptoms were first noticed following childbirth. One patient had used alcohol excessively for many years. In 1 instance there was a history of influenza one year before the onset of neurologic symptoms. In the rest of the records we were unable to find mention of any of the other suggested precipitating or causative factors. The occupation of none of the patients was such as to expose them to the action of metallic poisons, and in all the Wassermann tests were negative.

Wechsler[7] states that in the city of New York there are four times as many cases of multiple sclerosis in the foreign as in the native born, a statement which coincides with our findings. Two of our patients were German, 2 Irish, 1 Austrian, 1 Greek, 1 English, 1 Polish, 1 Italian and only 2 were native born. The disease is about twice as common in the white race as in the negro. All of the patients in our series were white.

The type of onset was gradual and insidious, and the disease was progressive in all the cases. Most of the patients did not present themselves for examination until they had had symptoms for several years. One of the most characteristic features of the course of disseminated sclerosis is the tendency to remissions. Five of our patients gave a history of one or more periods in which there was a marked retrogression or entire disappearance of symptoms. There was no migration of symptoms following a remission, as has been noted by some observers.

Charcot's triad of symptoms, nystagmus, intention tremor and scanning speech, was present in only 4 instances. Six of the patients showed nystagmus; 6 had intention tremor; 6 had slurring or scanning speech. The two symptoms however, which were present consistently in all except 1 of the cases, were absent abdominal reflexes and weakness of the lower extremities. In 7 instances sensory disturbances were noted, usually a diminution or loss of joint and muscle sensation. Eyeground examinations disclosed partial optic atrophy, often limited to the temporal side of the disk, in 6 of the subjects. In none of the cases was there a history of convulsions.

The blood and spinal fluid Wassermanns were negative in all cases. The blood chemistry was normal throughout, except that hyperglycemia was present in 1 patient. The spinal-fluid findings in multiple sclerosis are usually not entirely negative. If we accept 6 as the maximum number of cells per cubic millimeter in normal

spinal fluid, it will be seen in the following table that in three specimens there was a slight pleocytosis. The increase in the number of cells, when present, is never marked; in fact a count higher than 40 should, according to Ayer and Foster,[10] lead one to seek another diagnosis. The above observers believe that there are no spinal-fluid findings which are pathognomonic of multiple sclerosis, but in a study of 33 cases in which the clinical diagnosis was well established, they found "paretic" colloidal-gold curves in 50 per cent, and "luetic" curves in 25 per cent; 9 fluids out of 31 gave a positive test for globulin. The colloidal-gold curves in 2 of our cases were of the "paretic" type, and 3 of the "luetic." Three specimens showed a trace of globulin.

THE SPINAL FLUID IN TEN VERIFIED CASES OF MULTIPLE SCLEROSIS.

Case No.	Globulin.	Cells.	Colloidal gold.
1	Trace	19	4444311000
2	Negative	6	0000000000
3	Negative	0	2234321000
4	Negative	0	1133431100
5	Negative	0	2234442000
	Negative	2	0000000000
6	Negative	0	5555542100
7	Negative	20	0000000000
11	Trace	0	0000000000
12	Trace	10	0011100000

The following are the résumés of those cases in our series in which the clinical diagnosis of multiple sclerosis was confirmed at necropsy.

Case Reports. CASE I.—Georgia S., a Greek woman, aged twenty-four years, cigar maker by occupation, was admitted to the hospital, February 12, 1924, complaining of weakness and inability to walk. Two years before, she had begun to have gradually increasing weakness of the legs and one year later her hands began to shake. She had occasional incontinence of urine, and attacks of vertigo for the last few months. She had had influenza three years before admission, and since that time her menstruation had been irregular.

Neurologic examination showed choreiform movements of the arms and with constant tremor of the lower extremities. Ataxia of the upper limbs was present and there was scanning speech. There was a spastic paralysis of both lower extremities with evidences of pyramidal tract involvement, and the abdominal reflexes were absent.

Three months after admission her vision became poor. Eyeground examination showed pallor of the temporal side of the optic disks. Three months later she had horizontal and vertical nystagmus. Two years after admission there was advanced optic atrophy and the pupils reacted sluggishly to light. She became progressively weaker, gradually became demented, and died June 27, 1926.

Examination of the brain and spinal cord at necropsy showed a thickened pia arachnoid. There was atrophy of the cortex, especially that of the frontal and left parietal lobes, and a moderate degree of edema was present. Scattered indiscriminately throughout the brain and spinal cord were numerous areas of light brownish-gray color. These ranged in size from a few millimeters to 2 cm. in diameter, and in the brain were found more

frequently on the right side. Some of the plaques were definitely degenerated, with softening and cavitation. Under the microscope the above areas were seen to consist of irregular demyelinated patches, with neuroglia replacement. Many of the plaques were in an acute stage, as shown by a perivascular round-cell infiltration.

CASE II.—Pietro P., an Italian, aged thirty-four years, a hat maker by occupation, was admitted January 4, 1921, complaining of weakness, and pain in the face and legs. For the past seven years he had noticed weakness of the legs, which for the past three years had necessitated the use of a cane in walking. He also had shooting pains in the lower extremities and had been considered a case of tabes dorsalis. The pain in the "face" was really in his throat; it was of recent origin and caused difficulty in swallowing. He had used alcohol to excess for many years.

On physical examination he was found to have Ludwig's angina, and appropriate treatment was instituted. A depression of the skull in the left occipital region from an old injury was also noted.

Neurologic examination revealed a positive Romberg, and his gait was ataxic and spastic. Speech was slurring. The deep reflexes were exaggerated in both lower extremities, with bilateral Babinski and ankle clonus. The triceps and biceps reflexes were absent on the left. Both legs were spastic, more on the right, but the muscle power was fair. There was paraesthesia of the lower extremities. Four months after admission he showed nystagmus, the left pupil was larger than the right, and both pupils reacted sluggishly to light and were irregular. His condition became progressively worse without remissions. In 1923 he had developed tremor of the head, intention tremor of the upper extremities, incontinence and absent abdominal reflexes. He died March 7, 1926.

At necropsy, the brain showed moderate cortical atrophy, with superimposed edema. The pia was cloudy in the sulci. The ventricles were slightly dilated. Throughout the brain and cord there were sharply defined, almost translucent patches, varying in size from 1 mm. to 1 cm. in diameter. These areas were most numerous about the ventricles, but appeared in both the gray and the white matter. The plaques were very numerous in the pons, but less so in the medulla and midbrain, and only a few were found in the cerebellum. The spinal cord was slightly smaller than usual, but was otherwise grossly normal. Weigert-stained sections of the spinal cord showed the characteristic patches of multiple sclerosis. In the midbrain were seen recently involved areas with marked round-cell accumulation in the tissues about the vessels. No patches were seen in the cortical sections examined.

CASE III.—Emilie H., a white American female, aged thirty-five years, was admitted to the Episcopal Hospital August 7, 1924, complaining of inability to walk. Seven years prior to admission there was stiffness of her legs and arms. Her head began to "wobble," and she noticed that her speech had become monotonous. For the last three or four years, she had had great difficulty in reading. She later developed dysphagia. She gave a history of influenza in 1918.

In the neurologic examination, the patient was noticed to have a mask-like expression and was emotionally unstable. There was a coarse effort tremor of limbs so that she was unable to touch her nose with either hand. Her speech was scanning. The deep reflexes of both lower extremities were exaggerated, with bilateral Babinski and ankle clonus. The abdominal reflexes were absent. There was spasticity of the right arm and its muscles frequently went into clonic contractions. Spasticity and weakness were present in both lower extremities. Heat sense was lost on the inner

side of the left thigh, and in small patchy areas on the left side of the abdomen and chest. The left pupil was larger than the right and there was paralysis of the internal rectus of both eyes. Partial optic atrophy and lateral nystagmus were present. The tongue was tremulous and deviated to the right.

She developed paraesthesia of right side of face, became progressively weaker and died February 1, 1925.

The brain, at necropsy, was found to be small, and the pia arachnoid was slightly thickened. Plaque formation was seen on section of the cerebral hemispheres, pons, medulla, cerebellar hemispheres, midbrain and spinal cord. Microscopically, the plaques were seen to consist of irregular areas of demyelinization. Cell stains showed that the integrity of the ganglion cells of the cord was retained, even in the midst of the sclerotic patches.

CASE IV.—Marie S., housewife, aged forty years, Austrian by birth, came to the hospital October 13, 1921, complaining of weakness and unsteadiness of the legs and pain in the back and stomach. Weakness first started in the feet five years before admission, became progressively worse, and finally involved the entire lower extremities. She had had pain in the sacroiliac region for one year.

The following are the findings in successive neurologic examinations over a period of three years: The Romberg sign was positive and there was dysmetria of arms. The gait was ataxic and spastic with hyperreflexia, positive Babinski sign and clonus. Speech was monotonous and slurring. There was disturbance of heat and cold sensations below the seventh dorsal segment, and vibratory and muscle tendon sensations were lost in the legs. The abdominal reflexes were absent. Vision was impaired and fundus examination showed partial optic atrophy. The right pupil was larger than left; both pupils were regular but reacted sluggishly to light and in accommodation. Lateral nystagmus was present. The patient later became incontinent of urine and feces. Fibrillary twitchings occurred over the chest and abdomen. The muscles of the legs became markedly atrophied. She died March 12, 1926.

At necropsy the brain was soft and edematous, and the cortex was atrophied. The lower thoracic cord was flattened and soft. On sectioning the brain, the ventricles were found to be dilated, and many scattered gelatinous plaques were apparent. The plaques were distributed throughout practically the entire brain, and were even more numerous in the spinal cord. Stained sections showed sharply demarcated demyelinated areas, irregular in outline, corresponding to the lesions noted in the gross examination.

CASE V.—Mary P., A Polish housewife, aged forty years, came into the hospital on April 17, 1920, complaining of loss of power in the legs. Ever since the birth of a child eight years before, she had been troubled with weakness of the legs and shaking of the head and hands. She had had some symptoms ever since the onset, but there were periodical exacerbations, when all her symptoms grew worse and she was confined to bed. Each attack was more severe than the preceding one, and lasted longer. She had been in bed for six months during the present attack.

Neurologic examination showed an intention tremor of the arms and head. There was a tendency toward scanning speech. The deep reflexes of the lower extremities were exaggerated, with bilateral Babinski. There was weakness of the upper extremities and spastic paralysis of the lower. The abdominal reflexes were absent. Fundus examination showed bilateral partial optic atrophy. She later developed contractures of the lower extremities, gradually became weaker, and died June 21, 1923.

The brain and spinal cord at necropsy were apparently normal with the exception of many irregular, grayish patches of sclerosis which were scattered throughout. Microscopically these areas were found to be demyelinated plaques, showing no secondary degeneration.

CASE VI.—Harry F., a white, American machinist, aged fifty-two years, was admitted July 12, 1922, complaining of weakness of the legs. Two years previously, the patient had begun to experience intermittent pain in his legs. Shortly after this his legs began gradually to grow weak. For the past year he had been unable to walk, and for six months had been incontinent of urine. He had also noted some speech difficulty, and forgetfulness.

Neurologic examination showed a slight action tremor and the speech suggested scanning. The deep reflexes of the lower extremities were exaggerated, with bilateral Babinski and patellar clonus. The abdominal and cremasteric reflexes were absent and there was loss of position and vibratory sense in the lower extremities. Impaired vision without fundus changes, and lateral nystagmus were present. The pupils reacted sluggishly to light and in accommodation.

He gradually became weaker, showed no further neurologic changes and died November 14, 1922.

At necropsy, the fissures of the frontal lobes were moderately widened and deepened. The pia over the cortex was thickened and contained a small amount of fluid. The bloodvessels of the cortex were congested, and in some places there was extravasation of blood beneath the pia. In the center of the floor of the right lateral ventricle there was a small white patch. A similar, gelatinous, area was found in the cervical region of the spinal cord, extending about 1 mm. into the white matter. Sections of the brain and cord showed, under the microscope, many sharply outlined patches of myelin sheath degeneration, with neuroglia replacement. There were no signs of inflammation and no funicular degeneration.

CASE VII.—Arthur P., an English accountant, aged thirty-six years, came into the Episcopal Hospital, complaining of loss of power in the legs, of two years' duration. He was admitted February 21, 1924. One month before the onset of symptoms, he had fallen and twisted his back. Weakness began in the right leg, and at first was present only at intervals. At times his leg would drag, and at other times he walked normally. The attacks became more frequent, and the loss of power greater until finally he was unable to use his right leg. Two years after the onset of the above symptoms his left leg became affected in the same way, becoming progressively worse, with remissions, until both legs were paralyzed. He then experienced relatively good health, and went back to work; but after a short period his symptoms returned as before. In addition, he developed some tingling and numbness of both lower extremities. Six months before admission he became incontinent of urine and feces. Three weeks before admission he placed a hot-water bottle at his back one night and on removing it found that he had sustained a severe burn, although he had felt no pain.

The patient showed ataxic tremor of both hands in finger-to-nose test, also complete motor paralysis of the lower extremities with atrophy, extreme spasticity, ankle clonus and Babinski. The thenar and hypothenar eminences were wasted. The abdominal and cremasteric reflexes were lost and there was loss of pain, touch, temperature and position sensations up to the nipple line. Diminution of pain, heat and cold were present along ulnar border of both hands and arms with astereognosis and loss of position sense in both hands. Lateral nystagmus was found. He gradually became weaker and died March 21, 1924.

The brain at necropsy was very pale and the convolutions were flattened. The pia arachnoid had lost its normal luster, but was not thickened. The spinal cord presented no gross abnormalities, but was very small. Microscopic examination of sections of the brain revealed only one plaque, but this was large and very characteristic of multiple sclerosis. In the cord, the plaques were numerous, and occupied mainly the anterior and lateral portions, without much involvement of the posterior columns.

CASE VIII.—Maxwell S., a German machinist, aged twenty-three years, was admitted to the hospital April 11, 1915, complaining of blindness, and weakness of the legs. Three years previously he had become suddenly blind, but had two periods of remission in which his sight partially returned. Six months before admission his left leg and arm became weak and numb, and he dragged his leg in walking. His right leg became involved soon after, but never became as weak as the left. He had had trouble with his speech for four years.

Neurologic examination showed intention tremor and scanning speech. The patellar and Achilles reflexes were increased with positive Babinski. The biceps and triceps reflexes were bilaterally diminished. The lower extremities were spastic; the upper flaccid. There was atrophy of the shoulder girdle. The abdominal reflexes were absent, and there was flattening of the left side of the face. He could not move his legs and could hold up his left arm for only a few seconds. He could see light, but the eyeground examination revealed advanced optic atrophy. The pupils were large, irregular and the left was larger than the right. Both reacted sluggishly to light and there was loss of convergence with weakness of the right internal rectus. Lateral nystagmus was present. Contractures of the legs occurred later. He died June 16, 1921.

In the examination of the brain and spinal cord at necropsy, the pia was found to be thickened in the interpeduncular space, the brain was edematous and the bloodvessels were congested. Over the anterior surface of the pons two small grayish patches were observed. The same type of grayish area was seen scattered throughout the spinal cord, most frequently appearing on the posterior surface. On cut surface, the cord showed areas of sclerosis, dull gray in color, which were sometimes continuous with the gray matter, but at other times were entirely distinct from it. The bloodvessels of the cord were distended. Microscopically the sclerotic areas consisted of demyelinated plaques, with no secondary degeneration.

Comment. It will be noted in the above histories that although remissions are characteristic of multiple sclerosis, they occur as a rule only in the early stages. When paraplegia with spasticity and contractures set in, it is rare to see any retrogression of symptoms. Remission in any or all of the symptoms may occur, and a striking feature in the records reviewed is the number of times some of the patients have left the hospital and gone out to take up their former occupation, only to come back in a few weeks or months, complaining of the same symptoms as before. Optic atrophy in multiple sclerosis is usually not complete and in the early stages there may be a temporary improvement of vision, as is noted in 2 of the case résumés above.

Charcot's triad is no longer considered necessary for the diagnosis of disseminated sclerosis, and the importance of this change of

attitude is made doubly clear by a glance at the chief complaint which our patients gave on admission. What brought practically all of our patients to the hospital was not tremor and not speech disturbances, but weakness of the lower extremities. Charcot's triad in most cases never appeared at all, and when some of these symptoms did occur, in many instances it was only relatively late in the course of the disease. There is no one pathognomonic symptom of multiple sclerosis, but the onset of paraplegia in a subject in the second or third decade of life should cause a careful search for other symptoms, and most especially, for absent abdominal reflexes.

The disease with which multiple sclerosis is most frequently confused is cerebrospinal syphilis. Both are diseases of multiple lesions and multiple symptomatology. The types of multiple sclerosis sometimes differentiated, spinal, bulbar, cerebral, cerebellar and hemiplegic, may be duplicated by cerebrospinal syphilis. Both attack patients at about the same age, and both have a tendency to remissions. Both diseases frequently produce paraplegia, and both often affect the posterior columns. The characteristic ocular muscle palsies of syphilis may be paralleled by multiple sclerosis. Nystagmus, tremor and dysarthria may all be found when syphilis involves the brain stem and cerebellum.

It might be of interest at this point to review a case of cerebrospinal syphilis in which a diagnosis of multiple sclerosis was made clinically.

Case IX.—Thomas C., a white male American, aged twenty-one years, occupation, clerk, was admitted April 26, 1918, complaining of tremors of the entire body. The onset was three weeks previously with a feeling of "nervousness." He noticed difficulty in coördinated movements at that time. His subjective condition became progressively worse, and he developed tremors of his hands and head, which later involved all four extremities.

On neurologic examination, an intention tremor of the hands and head was found. Coördination was poor in the arms and legs and the left upper and both lower extremities were spastic. The speech was "sing-song" in character. All the deep reflexes were increased, on the left side more than on the right, and there was bilateral patellar clonus. The left arm was atrophied. The abdominal reflexes were present. Pain sense was diminished over the trunk. There was a suggestion of nystagmus, and slight exophthalmos and ptosis of both eyelids. The pupils were irregular and fixed to light and in accommodation. The nerve heads were pale. The tongue was tremulous. Bilateral eighth-nerve deafness was present.

Over a period of five years, the patient gradually became demented, lost weight and developed incontinence of urine and feces. During his period in the hospital he received neoarsphenamin by the Swift-Ellis method. His left side became totally paralyzed and he died June 25, 1923.

The blood and spinal fluid Wassermann was 4+ in both antigens. The blood chemistry was normal. The colloidal-gold curve was as follows: 3555542100.

At necropsy, the meninges were found to be thickened, especially at the base of the brain. This was found to be due to an infiltration with lympho-

cytes and plasma cells. The cortex showed many small areas where the ganglion cells were diminished in number. In the cord, the outstanding feature was an intense adherance and thickening of all the membranes, a pachyleptomeningitis, with lymphocytic infiltration and fibrosis of the dura. The cord itself was apparently involved only through pressure. Some of the nerve roots were also compressed by sclerotic tissue.

In the differential diagnosis of multiple sclerosis and cerebrospinal syphilis, the serologic study is of the utmost importance. When a diagnosis of syphilis is made in the absence of a positive Wassermann reaction in the spinal fluid, and the patient has received no treatment, such a diagnosis is almost invariably erroneous. On the other hand we do not wish to depreciate the value of the clinical findings, and it is by no means true that because the patient has positive serologic findings his neurologic symptoms are necessarily due to syphilis. In cerebrospinal syphilis the cells of the spinal fluid may be increased more than in multiple sclerosis, and globulin is more commonly present. The colloidal-gold curve is of slight differential value. From a clinical viewpoint, in spite of the potentially similar neurologic findings, the pupillary reactions present a valuable diagnostic feature; the Argyll-Robertson pupil is practically never present in multiple sclerosis.

Tumor of the cerebellopontine angle also at times presents a confusing picture. Headache, vomiting and failing vision, although constituting the cardinal symptoms of brain tumor, may also be present in disseminated sclerosis, but when the first two symptoms occur they are usually features of the earlier stages of the disease. Nystagmus and ataxia may occur in both conditions. Below is presented a case of fibroma of the left cerebellopontine angle which had been diagnosed multiple sclerosis.

Case X.—Eva V., an American housewife, aged forty-seven years, was admitted to the hospital July 21, 1926, complaining of weakness and inability to walk. One year previously she developed occasional attacks of weakness which had caused her to stop work. She also had occasional vomiting, not related to meals. She began to be troubled by attacks of headache and vertigo, and about six months later, her vision began to fail. The weakness of the lower extremities gradually progressed, and two months before admission she was unable to walk. The patient was lethargic and stuporous, with a masklike facial expression. She showed intention tremor of the upper extremities and slurring, indistinct speech. The deep reflexes were increased on the right side, with a positive Babinski sign. The abdominal reflexes were absent and there was weakness of all four extremities, most marked in the legs. Her vision was almost entirely gone and she showed lateral nystagmus. Hearing was impaired in the left ear.

The patient gradually became weaker and died July 24, 1926, three days after admission.

At necropsy, the brain surface was almost flat, and the convolutions were widened. A pear-shaped, cystic growth, 5 by 4 by 3 cm. in size, lay pressing upon the left side of the pons and imbedding itself in the left cerebellar hemisphere. Part of the anterior portion of the hemisphere had been destroyed. Microscopic examination showed the neoplasm to be a fibroma.

An important differential point between multiple sclerosis and angle tumor is the frequency of the symptoms of eighth nerve involvement in the latter. The optic disk change in multiple sclerosis consists of a degeneration, often limited to the temporal side, whereas in brain tumor there is usually a papilledema. Neoplasm is not characterized by remissions, and usually does not produce a paraplegia and absent abdominal reflexes.

A disease which manifests paraplegia and loss of deep muscle and tendon sense, and which is apt to be mistaken for multiple sclerosis, is posterolateral sclerosis. As a rule, however, in the advanced stage of disseminated sclerosis the sensory disturbances are slight compared to the amount of paralysis. The following case was diagnosed posterolateral sclerosis, a fact which is not surprising, considering the absence of characteristic symptoms of multiple sclerosis.

CASE XI.—Callum M., an Irishman, aged sixty-five years, was admitted to the hospital for a lesion of the left eye, which was found to be carcinoma of the orbit. His left arm and leg had been stiff for twelve years. He denied ever having had a stroke.

The left arm and leg showed weakness and spasticity, with increased deep reflexes, but no clonus or positive Babinski sign. His right patellar reflex was somewhat exaggerated. There was absence of pain sense over both legs and slight impairment over the abdomen. Temperature sense was impaired over the lower part of the left leg, and the sense of position was lost in both legs.

He became progressively weaker and died March 7, 1926, one month after admission.

The brain, at necropsy, was edematous, and the convolutions of the cerebral hemispheres presented moderate atrophy. The cord was flattened, and showed on section a sclerosis of the posterior columns. The pia arachnoid, under the microscope, was seen to be definitely thickened, but not infiltrated. The cortex showed a few foci where the ganglion cells were diminished in number. The small vessels were thickened, and many had hyalinized walls. The larger vessels showed a slight intimal proliferation. Much amyloid material was present in the cord, especially in the posterior columns. Weigert-stained sections showed many irregular, demyelinated areas in nonanatomic locations, but being most numerous in the thoracic and lumbar regions of the cord.

Emotional changes sometimes occur in multiple sclerosis, being due, according to some authorities, to lesions in the thalamus. The following is a case in which emotional disturbance was a cardinal feature.

CASE XII.—Fredericka I., a German housewife, aged forty-five years, was admitted to the hospital March 10, 1921, complaining of nervousness. Fifteen years before admission she noticed that she had some speech difficulty. Tremor developed in the right upper extremity, and soon after appeared on the left side. Nine years before admission she began to have difficulty in walking, and showed some emotional disturbance, with a silly, causeless laugh. There were no remissions, and the paralysis of the lower extremities was gradually progressive, so that she was unable to walk without support.

The patient was emotional, talkative and overactive. She showed: tremor of the head at rest, increased by emotion; suggestion of intention tremor of the upper extremities; torticollis and twisting of trunk. Her speech suggested the scanning type. The reflexes were increased in both lower extremities, with positive Babinski. The gait was spastic, and muscle power was poor in the legs. The abdominal reflexes were absent. Her pupils were irregular, the left was larger than the right but both reacted to light and in accommodation normally.

The patient gradually became weaker and more emotional, with frequent causeless laughs. Her memory deteriorated and the tremors became more pronounced with increase of tortipelvis and paralysis. She died April 11, 1925. The clinical diagnosis was dystonia musculorum deformans (?).

The brain was very small, even for a female specimen, weighing 980 gm. The cerebral hemispheres showed moderate convolutional atrophy. The pia arachnoid was thickened, especially over the left frontal and parietal lobes. Sectioning of the brain disclosed areas, brownish in the portions adjacent to the ventricular system, grayish in other portions, scattered throughout. The globus pallidus on the left side was much more affected than on the right. The caudate nuclei were shrunken, and the corpus callosum was very small. Adjacent to the anterior horn of the lateral ventricle in the left occipital lobe was an immense area of grayish discoloration which followed the horn to its extremity. The ventricular system was moderately dilated. The same type of grayish areas were found in sections of the spinal cord. Microscopically the areas described above were found to be irregular, demyelinated plaques, in which there was an increase of neuroglia. In some areas there was a tendency toward a perivascular round-cell infiltration.

Among other conditions which may offer some difficulty in differential diagnosis are cerebral arteriosclerosis and hysteria. One of the cases which we studied, diagnosed multiple sclerosis, was found at necropsy to show arteriosclerosis of the cerebral vessels. Hysteria and multiple sclerosis both exhibit remissions and variable symptoms, but in the former there may be contracted visual fields, or disturbances in sensation such as "glove" and "stocking" anesthesia. Rarely lethargic encephalitis may cause confusion in differentiation.

PATHOLOGIC NOTES (by N. W. Winkelman, M.D.). Pathologically multiple sclerosis is characterized by irregular demyelinated plaques throughout both brain and spinal cord, showing an utter disregard for anatomic boundaries. They vary greatly in number; in 1 of the cases reported above, but a single plaque was found in the brain; in others they were countless. In the cerebrum, they show a predilection for locating beneath the ventricles. Each plaque consists of a demyelinated area in which axis cylinders can be demonstrated by appropriate staining methods. There is a sharp demarcation from the normal tissue in myelin sheath stains. A tendency to symmetry is noted. While the subject of etiology is obscure, inflammatory changes, as well as degeneration, are present, the former probably occurring only early in the disease. While secondary degeneration from the plaques is very rare, it does occur at times.

Summary and Conclusions. 1. During a period of six years, in the Philadelphia General Hospital, there were 38 cases diagnosed multiple sclerosis clinically, out of a total of 5469 neurologic admissions, an incidence of 7 per 1000.

2. In 1700 brain and cord examinations during the same six-year period, the lesions of multiple sclerosis were found in 9 instances (5.3 per 1000). In 2 of these cases the clinical diagnosis had been incorrect, giving an error in diagnosis of 22 per cent. Multiple sclerosis was overdiagnosed in 2 cases, also showing 22 per cent error.

3. An analysis of 11 verified cases of multiple sclerosis has been presented, with a résumé of the history and neurologic findings in 10. The ratio of males to females in our series was 6 to 5. The average age of onset was found to be thirty-four years. The average age of death was forty-one and a half years. The average duration of the disease was nine years. There were possible etiologic or precipitating factors in 5 cases; injury in 2, alcoholism, childbirth and influenza. In all there was a gradual onset and progression of symptoms, with remission in 5 cases. The remissions, in all cases, occurred only in the early stages of the disease. The two symptoms which were present in all but 1 case were paraplegia and absent abdominal reflexes. Sensory disturbances were noted in 7 patients and were mainly of the posterior column type. Charcot's triad was present in only 4 instances, and should not be required for a diagnosis. Optic atrophy was present in 6 cases, but in no case was it complete.

4. As for the spinal fluid there was a "paretic" curve in 2 cases, and a "luetic" curve in 3. Globulin was present in 3 cases. The highest cell count was 20.

5. In differential diagnosis, multiple sclerosis is most commonly confused with cerebrospinal syphilis, brain tumor, especially tumor of the cerebellopontine angle, posterolateral sclerosis, arteriosclerosis of the cerebral vessels, hysteria and encephalitis.

6. Pathologically multiple sclerosis is easily recognized by its irregular, demyelinated areas throughout the brain and cord.

NOTE.—We are indebted to Drs. J. W. McConnell, C. S. Potts, D. J. McCarthy, John B. Carnett, T. H. Weisenburg, W. G. Spiller and George Wilson for permission to use the data on their cases in this report. We also wish to thank Dr. N. W. Winkelman and Dr. George Wilson for many helpful suggestions.

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VENOUS PRESSURE AS A GUIDE TO VENESECTION IN CONGESTIVE HEART FAILURE.

By J. A. E. Eyster, M.D.,

AND

William S. Middleton, M.D.,

MADISON, WIS.

(From the Department of Medicine, University of Wisconsin.)

Few empirical therapeutic procedures have weathered the scrutiny of modern science. Venesection, for example, had enjoyed a period of unexcelled favor from the earliest dawn of medicine until the awakening of the scientific spirit in the French school of the early nineteenth century. And singularly the most active period of leeching and phlebotomy, through the energetic precepts of Broussais, Rasori and Benjamin Rush, immediately preceded the convincing statistical evidence of Louis against indiscriminate bloodletting in pneumonia. Apparently the profession had been prepared for such a revelation, since the reaction carried venesection into almost complete oblivion until very recent years.

Numerous indications have from time to time been stated for bloodletting. With improved methods of study it would seem advisable to subject each and all of these indications to scientific proof before reviving a method of doubtful value. In the case of cardiac decompensation, a measure of right heart efficiency, primarily, exists in the venous pressure determination. Ultimately this factor becomes a measurement of myocardial competency in general.

According to the modern theory, the return flow of blood to the heart determines the output of the ventricles; and since the degree of diastolic filling establishes the initial load of ventricular contraction, within certain limits the heart responds to an increased load by increased work. The extent of the myocardial ability to so react

constitutes cardiac reserve; and when the initial load or the venous pressure exceeds the ability of the heart to so react, cardiac decompensation results.[1] In a word, the ventricles are unable to meet the load of venous pressure, and responding by ineffectual contraction, dilatation ensues, the venous pressure mounts and the margin of expendible force or reserve is still further narrowed. Ultimately the picture of congestive heart failure becomes more or less complete.

The importance of venous pressure determinations in cardiac decompensation was first emphasized by Hooker and Eyster in 1908.[2] Clark later (1915)[3] arbitrarily fixed 20 cm. of water as the critical level of venous pressure in cardiac decompensation. The prognostic value of the trend of the venous pressure curve received due attention. In addition to confirming these important points, Eyster and Middleton[1] concluded from extensive studies that the normal venous pressure never exceeds 11 cm. in the recumbent position. Eliminating the unusual cases of phlebosclerosis and local interference with venous return, an elevated venous pressure is *prima facie* evidence of cardiac decompensation.

Gordon[4] has established by roentgenologic studies a decrease in the silhouette area of the heart in such cases of cardiac decompensation as responded favorably to venesection. A parallelism between decreasing heart size and falling venous pressure with regained compensation had been previously pointed out by Eyster and Middleton.[1] The inferred importance of routine venous pressure observations both in prognosis and as a guide to the utilization and success of venesection in congestive heart failure, which has also been noted by Lemierre and Bernard,[5] led to the present study. Twenty-one cases of cardiac decompensation have been subjected to venesection. Dyspnea, orthopnea, Cheyne-Stokes respiration, cyanosis, cough, bloody frothy expectoration, pulmonary congestion and edema, positive centrifugal venous pulse, engorged pulsating liver and venous hypertension have been the criteria for decision in the matter of bloodletting. A venous pressure of 20 cm. of water which was ascending was the ultimate determining factor in the matter. As a rule 500 cc. of blood were withdrawn since Meek and Eyster[6] have demonstrated that the removal of approximately such an amount is necessary to effect a decrease in the heart size. The important data in the clinical records of the 21 cases are tabulated below.

This table requires little comment. The age range between thirty and seventy years (excepting cases 9 and 14) was characteristic of the type of case under consideration. The distribution of the sexes was preponderantly in favor of the male. The basic lesion was about evenly divided between primary endocarditis and hypertensive myocardial degeneration. The figures relative to etiology did not permit of gross generalization. Sixteen of the cases gave his-

CLINICAL DATA ON VENESECTED CASES.

	Age.	Sex.	Basic lesion.	Etiology.	Decompensated.		V. P.	Amount blood let.	Resultant V. P.			Effect.	
					Remote.	Present.			Lowest.	Interval.	Duration.	Immediate.	Ultimate.
1	64	M.	Myocardial degeneration	Hypertension; arteriosclerosis	4 yrs.	Continued	21	400 cc.	14	30 min.	Maintained	Little change early	2 days later less cyanotic, less edema, diuresis.
2	62	M.	Myocardial degeneration	Hypertension; arteriosclerosis	7 mos.	1 mo.	20	350 cc.	15	24 hrs.	Maintained	Immediate improvement mental state and objectively	Death 5 months later, V. P. 13.
3	62	F.	Endocarditis	Rheumatic fever; arteriosclerosis	7 yrs.	6 mos.	20	500 cc.	10	24 hrs.	10 days later 16 cm.	Dyspnea lessened, output increased	Slump on 11th day, death on 33d day.
4	40	M.	Endocarditis	Rheumatic fever	3 yrs.	6 wks.	19–20	500 cc.	12	Immediate	5 hrs later 16 cm. 24 hr. later 19 cm.	Immediate subjective improvement in breathing, cyanosis same.	
									Three Days Later				
							21	500 cc.	14	Immediate	24 hrs. later 16 cm.	Early relief dyspnea cyanosis.	Died 36 hrs. after venesection.
5	55	M.	Myocardial degeneration	Arteriosclerosis with coronary involvement	1 yr.	2 wks.	Edema	500 cc.	Edema	.....	.....	No	Died 2 days later.
6	73	M.	Endocarditis	Rheumatic fever (?)	?	2 wks.	36	450 cc.	13	10 min.	1 hr. later 15 cm., 24 hrs. later 23 cm.	No response	Died 20 days later.
7	43	F.	Endocarditis	Scarlet fever	....	9 mos.	28	500 cc.	15	48 hrs.	3 days later 24 cm.	No response	Died 10 days later.
8	69	M.	Myocardial degeneration	Hypertension; arteriosclerosis	4 yrs.	2 mos.	26	500 cc.	14	Immediate	Irregular from Cheyne-Stokes, 13–20 cm. Steady fall	Less abdominal distress; improving subjectively	Remarkable return of circulatory balance; discharged 6 wks. later V. P. 10 cm.
9	17	M.	Adhesive pericarditis	Multiple serositis; rheumatic fever	1½ yrs.	6 mos.	20	300 cc.	11	Immediate	5 hrs. later 14 cm.	Marked subjective improvement	Progressive improvement; discharged 7 weeks.

10	51	M.	Endocarditis	Rheumatic fever (?)	2 yrs.	3 mos.	22	500 cc.	8	1 hr.	Not above 12 cm. until death	Less restless; less cough; less pulmonary congestion	Infarction determined death 11 days later.
11	54	M.	Myocardial degeneration	Hypertension; arteriosclerosis	2 yrs.	Continued	Edema	600 cc.	Edema	.....	.....	Pronounced subjective and objective improvement beginning in 24 hrs.	Death 6 wks. later from cerebral hemorrhage.
12	34	F.	Aortitis; myomyocardial degeneration	Syphilis	7 mos.	2 wks.	22	450 cc.	11	Immediate	.....	Slight but very temporary improvement	Death 27 hrs. later from pulmonary infarction.
13	45	M.	Endocarditis	?	....	1 mo.	25	500 cc.	12	48 hrs.	11–15 cm. until discharged	Marked subjective improvement	Discharged markedly improved 7 wks. later.
14	19	M.	Endocarditis	Rheumatic fever	10 mos.	Continued	20	350 cc.	17	24 hrs.	Steady fall to 13 cm. in 10 days	Marked subjective improvement	Death 12 days later.
15	43	M.	Myocardial degeneration	Hypertension; arteriosclerosis	9 yrs.	4 mos.	22	550 cc.	12	24 hrs.	5 days later 16 cm.	No improvement	
								Thirteen Days Later					
								550 cc.	....	.....	.....	No response	Death 2 days later.
16	36	M.	Endocarditis	Rheumatic fever	....	1 wk.	15	265 cc. (for pulmonary infarction)	12	30 min.	Fall to 7 cm. in 24 hrs.	Pronounced improvement in general condition, less cough	V. P. remained normal until discharge 6 wks. later.
17	65	M.	Endocarditis	Rheumatic fever	6 wks.	Continued	Edema	600 cc.	Edema	.....	.....	Marked subjective improvement	V. P. 10 cm. 11 days later; steady gain to discharge 5 wks later.
18	52	M.	Myocardial degeneration	Arteriosclerosis	....	Continued	20–22	500 cc. (convulsion with apoplexy)	13	3½ hrs.	Slight rise but fall to 12 in 24 hrs.	Apparent early improvement; later disappearance of cyanosis.	Sudden death 2½ wks. later.
19	51	M.	Myocardial degeneration	Hypertension; arteriosclerosis	6 mos.	1 wk.	18	350 cc.	16	Immediate	No real gain, 24 cm. 4 days later.	No response	
								Four Days Later					
							24–26	400 cc.	16	Immediate	12 hrs.	Definitely less dyspneic	Died 31 hrs. later.
20	75	M.	Myocardial degeneration	Arteriosclerosis	6 yrs.	2 wks.	24	500 cc.	11	2½ hrs.	24 hrs. later 21 cm.	No response	Died 2 days later.
21	50	M.	Myocardial degeneration	Arteriosclerosis	11 mos.	Continued	20	400 cc.	5	Immediate	1½ hrs., 2 hrs. later 8 cm.	Respiration less labored; fewer râles	Sudden collapse and death 8 days later.

tories of previous periods of decompensation, and the average duration (20 cases) of the present period of decompensation was 6.5 months. Immediate improvement was remarked in 15 of the 21 cases following venesection and no evident preëxistent circumstance of age, sex, basic lesion or etiology was operative in its determination. The antecedent height of the venous pressure was apparently without influence in this direction; and the degree of venous pressure fall bore no constant relation to the early improvement. In 6 cases, there was no apparent improvement from the venesection. Of these 6 cases, death occurred within forty-eight hours in 4, and in twenty and ten days, respectively, in the remaining 2.

The ultimate outcome of these cases was very unfavorable, 15 cases of the group dying in the hospital. However, a disproportionate length of life in those who showed immediate improvement was apparent. It would seem justifiable to regard cases that survived a

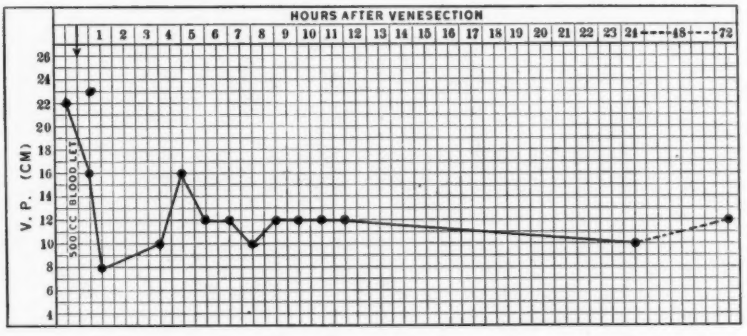

CHART I.

week, as rallied from the emergency which led to phlebotomy. Of those 9 cases in the entire group (2, 3, 6, 7, 10, 11, 14, 18, and 21) which survived venesection one week and later succumbed, 7 had shown early amelioration; and finally 4 of these 7 died of circulatory accidents, namely, pulmonary infarction, cerebral hemorrhage, and so forth. It may be affirmed then that in a group of 21 cases of cardiac decompensation venesection was attended by early improvement in 15. Subsequently, however, 9 of these 15 individuals died at intervals of from thirty-one hours to five months. The extremity in which the great majority of these cases was seen, is an important detail in determining the high mortality in spite of any form of treatment.

The immediate effect of venesection is to lessen the load of returning blood to the right heart. The effect is essentially mechanical. If the range within which the muscle is able to respond to an

increased load by increased work be sufficiently wide, this temporary, though slight, respite enables the muscle to contract more adequately. This circumstance will operate to maintain a lowered venous pressure, or toward compensation. Whereas if the range of physiologic response be too narrow or the withdrawal insufficient, the temporary lowering of venous pressure which invariably attends venesection in cardiac decompensation, is not maintained and the venous pressure steadily mounts to or above its antecedent level. Although at times venesection repeated at a considerable interval may renew an early satisfactory response, no number of bloodlettings will effect an amelioration of symptoms if the primary attempt has shown no movement in this direction. The most accurate guide to this circumstance is the venous pressure curve. If the heart muscle responds adequately to the reduced load, the venous pressure will remain low (Chart I) and the subjective and objective evidences of cardiac decompensation will subside. On the other hand, an early

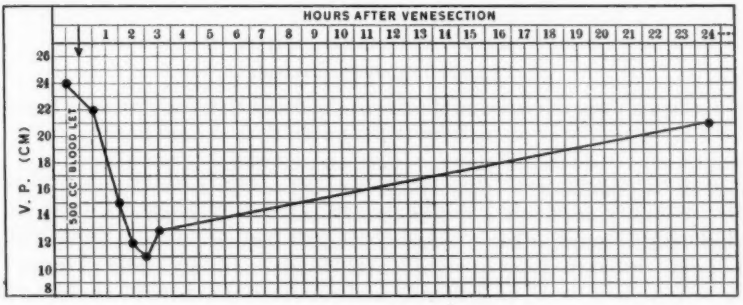

CHART II.

sharp rise in the venous pressure or a steady climbing to its original high level (Chart II) indicates a lack of myocardial reserve and no continued clinical improvement can be expected.

Conclusion. The value of venesection in congestive heart failure is reiterated. The low percentage of ultimate successes attendant upon its employment may in part depend upon the very unfavorable cases which are commonly selected as subjects. Unquestionably, the greater the cardiac reserve, the more probable the success of any form of therapy. This condition particularly applies when the therapeutic measure is a purely mechanical one as in venesection.

The venous pressure is an excellent index of the myocardial reserve, and venous hypertension in the absence of local causes results only from cardiac decompensation. Routine venous pressure determinations are, therefore, advised not only as a guide to venesection but also as a measure of its efficacy.

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THE RELATION BETWEEN CHOLESTEROLEMIA AND DEPOSITS OF CHOLESTEROL IN THE GALL BLADDER: AN EXPERIMENTAL STUDY.

By F. E. Blaisdell, M.D.,

and

L. R. Chandler, M.D.,

San Francisco, Calif.

(From the Laboratory of Surgical Research, Stanford University Medical School, San Francisco, Calif.)

A histologic study of the "strawberry gall bladder" as well as the evidence presented in the recent literature suggests that the cholesterol found in the walls of these gall bladders is of a metabolic, not an inflammatory origin. McMeans,[1] Bailey[2] and Dewey,[3] have fed cholesterol to animals, and reported deposits of cholesterol in the aorta, liver, spleen, kidney, adrenal and ovary. Dewey reports some fat, but no cholesterol, in the gall bladders of rabbits in his feeding experiments. We have found cholesterol deposited in the human aorta, spleen and liver in 3 strawberry gall bladder cases studied postmortem. The following experiments were done in order to determine, if possible, the relation between hypercholesterolemia, produced by feeding cholesterol, and the deposits of cholesterol in certain characteristic cells in the mucosa and submucosa of the gall bladder.

Fifteen rabbits and 10 dogs were used for the experiment. Blood cholesterol was determined in all the animals before the feeding was started, and at weekly intervals thereafter. The cholesterol determinations were made by the method described by F. L. Leiboff,[4] and are reported as milligrams per 100 cc. of blood. The cholesterol, emulsified in egg yolk, was fed to the rabbits daily, by gavage. Beginning with 0.1 gm. cholesterol and one egg yolk, the amount was doubled each week until each animal received 1 gm. cholesterol and one egg yolk per day. The rabbits were sacrificed at intervals varying from twenty to one hundred and forty-five days.

The cholesterol in gelatin capsules was fed to the dogs daily. Beginning with 0.2 gm., the cholesterol was increased weekly until each animal received 1.5 gm. per day. Five of the dogs (Series II) were operated on, and the cystic duct ligated, so that no bile could get into the gall bladder. The cystic artery and vein were not included in the ligature about the duct. The operations were done two weeks before the cholesterol feeding was started. The dogs were sacrificed at intervals varying from thirty-eight to one hundred and nineteen days.

Cultures were made from the gall bladder wall and the bile in the first 10 rabbits. As the results were negative in all 10 cases, this procedure was omitted in the remainder of the experiments.

The necropsies included the examination of the aorta, liver, spleen, kidney and adrenals, but special attention was paid to the gall bladder. The gall bladder was examined grossly with binocular dissection microscope, stained with Sudan III, with Nile-blue sulphate and sulphuric acid, and was examined with polarized light.

The results of the experiments are shown in the following charts and summaries.

CHART I.—RABBIT SERIES.

No.	No. days fed.	Cholesterol fed, gm.	Blood cholesterol.		Finish, mg.	Deposit in gall bladder wall.	
			Began, mg.	Highest, mg.		Epithelium.	Submucosa.
1 . .	20	1.9	91.0	222.0	222.0	–	–
2 . .	24	2.3	99.0	285.7	285.7	–	–
3 . .	42	6.0	120.0	238.1	151.5	–	–
4 . .	71	15.3	113.5	800.0	800.0	–	–
5 . .	79	17.3	91.5	285.7	146.0	–	–
6 . .	89	23.5	97.0	1250.0	1250.0	–	–
7 . .	105	30.0	86.0	851.0	540.5	–	–
8 . .	125	44.2	113.5	363.3	208.3	?	+
9 . .	125	44.2	129.5	975.6	869.6	–	–
10 . .	132	46.2	87.5	357.1	357.1	–	–
11 . .	33	13.1	61.7	378.8	378.8	–	–
12 . .	69	26.7	83.3	512.9	227.3	–	+
13 . .	104	52.1	86.9	1333.2	979.6	?	+
14 . .	145	86.1	74.6	1600.0	1600.0	?	–
15 . .	145	86.1	86.9	1428.0	1250.0	?	+

Summary of Rabbit Series. Eleven of the 15 rabbits had deposits of cholesterol in the aorta, liver, or kidney. These deposits were similar to those described by McMeans,[1] Bailey,[2] and Dewey.[3]

Except for a moderate desquamation of the epithelial cells in 6 of the gall bladders, they showed no evidence of inflammation.

Four of the rabbits had deposits of lipoid in the wall of the gall bladder. This lipoid was contained in the cytoplasm of large cells, with small reticular nuclei, lying in the stroma of the villi and submucosa. The lipoid stained greenish-blue with the Nile-

blue sulphate, terra cotta brown with concentrated sulphuric acid, and when viewed with crossed Nicol's prisms, it was doubly refractive. From these reactions we conclude that the lipoid contained cholesterol or its esters.

CHART II.—DOG SERIES I.

No.	No. days fed.	Cholesterol fed, gm.	Blood cholesterol.		Finish, mg.	Deposit in gall bladder wall.	
			Began, mg.	Highest, mg.		Epithelium.	Submucosa.
1 . .	98	58.4	89.0	256.0	124.0	+	+
2 . .	113	82.4	82.0	232.0	205.0	+	+
3 . .	119	91.4	109.5	174.0	128.5	+	+
4 . .	38	17.2	67.3	335.0	335.0	+	+
5 . .	62	34.4	80.8	214.0	170.0	+	+

SUMMARY. DOG SERIES I. None of the dogs in this series had deposits of cholesterol in the aorta, liver, spleen or kidney. None of the gall bladders showed any evidence of inflammation and the epithelium was well preserved in all of them. Microscopic examination showed that the epithelial cells of all the gall bladders in this series contained lipoid.

The lipoid appeared as globules in the cytoplasm at the base as well as the periphery of the cells. Also many lipoid-containing cells were seen in the stroma of the villi and in the submucosa. These cells were large, round or oval, with slightly granular nuclei. In some places they appeared separately, but usually were in groups of four or five, and seemed to be identical with the lipoid-bearing cells seen in "strawberry gall bladders." The lipoid, seen in frozen sections, appeared as globules in the cytoplasm of these cells, and stained a greenish-blue with Nile-blue sulphate, terra cotta brown with sulphuric acid, and when viewed with polarized light, most of it was doubly refractive. From these reactions we conclude that the lipoid contained cholesterol or its esters.

CHART III.—DOG SERIES II.

After Ligation of Cystic Duct.

No.	No. days fed.	Cholesterol fed, gm.	Blood cholesterol.		Finish, mg.	Deposit in gall bladder wall.	
			Began, mg.	Highest, mg.		Epithelium.	Submucosa.
6 . .	69	56.8	94.0	203.0	148.0	–	–
7 . .	56	40.0	176.0	279.0	134.0	–	–
8 . .	49	29.8	111.0	220.0	220.0	–	–
9 . .	56	38.8	119.0	235.0	138.0	–	–
10 . .	35	16.0	134.0	228.0	154.0	–	–

SUMMARY. DOG SERIES II. The 5 dogs in this series had been operated on and the cystic duct ligated two weeks before the cholesterol feeding was started. None of the dogs had deposits of cholesterol in the aorta, liver, spleen or kidney. In 1 case the liver edge, gall bladder and transverse colon were adherent to the operative wound in the anterior abdominal wall. In the other 4 cases the gall bladders were smooth and showed no evidence of inflammation. They all contained a little dark, thick, tenacious bile. In 4 cases microscopic examination showed a few small globules of lipoid in the cytoplasm of some of the epithelial cells. This lipoid-stained blue with Nile-blue sulphate and was not doubly refractive when viewed with polarized light. In none of the gall bladders was there any lipoid in the stroma or deeper layers of the gall bladder wall, and none of that seen in the epithelial cells could be identified as containing cholesterol.

Conclusions.—1. A hypercholesterolemia was produced in all animals by feeding cholesterol.

2. A continued hypercholesterolemia resulted in deposits of cholesterol containing fat in certain characteristic cells in the mucosa and submucosa of the gall bladder, when the cystic duct was patent. This occurred both in rabbits and dogs, but more readily in the latter.

3. When the cystic duct was ligated before feeding cholesterol, the hypercholesterolemia was produced, but no cholesterol-containing fat was found in the gall bladder wall, not even in the epithelium.

4. The deposits of cholesterol in the wall of the gall bladder are dependent upon absorption of cholesterol from the bile.

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MUCOUS COLITIS DUE TO FOOD ALLERGY.

WITH A REPORT OF FIVE CASES.

BY EDWARD HOLLANDER, M.D.,

GASTROENTEROLOGIST, MANHATTAN STATE HOSPITAL, NEW YORK CITY.

THE phenomenon of hypersensitiveness in experimental medicine has been known for a long time, but only in recent years, through the work of Walker, Cook, Longcope, Duke and others, has the subject been applied to clinical medicine. The successful applica-

tion of the principles of allergy to the analysis of such clinical entities as hay fever, asthma, urticaria and eczema has stimulated the extension of the subject to the study of other affections.[1, 2]

Allergy is a condition of altered reaction on the part of tissue cells to foreign chemical agents. The reactions are evidenced in those tissues that are vulnerable in the affected individual. The allergic reactions in the bronchi, nasopharynx and skin giving rise to asthma, hay fever, and urticaria are now well known. That the gastrointestinal mucosa may also react in an allergic manner causing chronic disorders of the gastrointestinal tract has not been so generally recognized nor so intensively studied.

In 1921 Duke[3] reported 6 cases in which severe gastrointestinal symptoms resulted from the ingestion of food to which the patients were hypersensitive. Recently Andresen[4] reported several cases in which food allergy caused gastrointestinal pain. The present paper is a report on 5 cases of mucous colitis in which hypersensitiveness to food proved to be the cause of the condition.

The term mucous colitis may be defined as a disease characterized by the formation in the colon of large quantities of abnormal mucus. The condition has been described under various names, the more commonly employed being: mucous colic, mucous diarrhea, membranous diarrhea, and membranous colitis.

The symptoms are pains along the course of the colon, gas distention, constipation frequently alternating with diarrhea and intestinal colic. These are associated with mental depression, neurotic manifestations or physical weakness. When the pains are present chiefly in the right lower quadrant or right upper quadrant of the abdomen, the condition is easily confused with disease of the appendix, gall bladder, or even peptic ulcer. The correct diagnosis is frequently missed since most patients do not notice or recognize the passage of mucus in the stools, and the sigmoidoscope is not generally employed in a routine examination. As a result these patients are frequently classed as neurasthenics or psychoneurotics. In some cases paroxysms of severe colic occur due to tenacious mucus adhering to the colon and inducing spasm. The mucus is usually passed in small, brown, jelly-like masses or strands, but sometimes in tough pseudomembranes forming long casts of the bowels, resembling a tapeworm. These casts consist entirely of mucus with a few enmeshed degenerated epithelial cells and leukocytes. No fibrin is present. In the sigmoidoscope the mucosa appears dry and glazed with inspissated mucus adherent to it. Mechanical removal of the tenacious mucus is sometimes difficult, and like a scab, may leave a bleeding area. On physical examination, the entire colon, or part or it, may be palpable and tender to pressure.

There is no constant pathologic anatomic basis for the disease; necropsies are rare since the condition is not fatal. Usually no recognizable lesion is found, but in some cases the mucous membrane of the colon reveals small areas of inflammation.

The etiology of the disease has not been definitely determined. One theory ascribes the condition to a secretory neurosis of the colon without any anatomic basis (similar to asthma). Another view holds that the disease is a true catarrhal inflammation confined to small areas of the mucous membrane. The condition may occur at all ages, but more often between the years of twenty and forty. It occurs more frequently in persons of nervous temperament, especially women, and it tends to run in families. Constipation and enteroptosis are considered important predisposing causes.

The treatment usually employed consists in the removal of foci of infection, colon irrigations, acidophilic bacterial implantation, correction of ptosis by mechanical support, bland protein diet and sedative medication. In the 5 cases I am reporting such measures failed to give more than temporary relief. The clinical picture disappeared only after the omission of foods to which the patients were sensitized, and it reappeared when the foods were ingested, indicating that food allergy was the cause of the mucous colitis in these cases.

The method employed to detect the presence of sensitization is dependent upon a local reaction following the application or injection of foreign substance within the epidermis. In this manner more than 50 per cent of cases of hypersensitiveness can be detected. However, the mere presence of a local dermal test is not sufficient proof that the symptoms of a case are due to an allergic condition. Cook and Vander Veer found that skin sensitiveness was present in 14.5 per cent of normal people. The proof of relationship between hypersensitiveness and clinical symptoms must depend, in the last analysis, not alone on positive dermal tests but also on the disappearance of the symptoms when the offending material is withdrawn, or if that is impossible, when immunity can be established by methods of desensitization. In addition to the phenomenon of sensitization, mechanical factors must also be considered. When a mucous membrane is sensitized it is in an irritable state and besides the allergic factor, coarse substances may cause symptoms from mere mechanical irritation. Thus, without the use of skin tests, it would be difficult to say which food played the rôle of allergen or which that of mechanical irritant.

In the following cases the dermal tests were performed by the scratch method, using seventy-five of the more common foods. When the complaints are of a continuous nature uncommon articles of food need not be tested. If a food that is ingested infrequently were to sensitize a person the symptoms resulting would be periodic and the food at fault could be easily ascertained. However, if one is sensitive to foods occurring in the daily diet, such as wheat or milk, symptoms of a chronic nature would result and the particular foods could not be detected by the patient.

Each patient was studied by the technical methods of gastric analysis, roentgenology of the gastrointestinal tract biliary drainage.

and sigmoidoscopy, including a microscopic examination of the mucus or fecal contents present. For brevity of report only abnormal findings are mentioned.

Case Reports.. CASE I.—Miss A. M., aged twenty years, occupation, office work.

Past History. Appendectomy was performed for acute appendicitis twelve years previous.

Present history was four years in duration. The symptoms consisted of constant cramplike pains, shifting over the entire abdomen, associated with anorexia, nausea and flatulence. The bowels were usually constipated but alternated with diarrhea, when large amounts of mucus were passed in the stools. Various medical treatments were tried but they failed to relieve her symptoms. She observed that when she avoided food entirely her abdominal pains disappeared, so at one time, in desperation, she placed herself on a fast lasting eleven days. During this period she was entirely free from her complaints and except for weakness she felt entirely well. On resuming food her symptoms returned.

Physical Examination. The patient was a slender neurotic young woman of asthenic habitus. The colon was palpable, spastic and tender throughout its entire course.

Technical Examinations. Sigmoidoscopy revealed a dull congested mucosa entirely covered with large membranes of inspissated gray mucus. This was so adherent that mechanical removal was difficult. In some areas, removal of the mucus, like a scab, left a bleeding area.

Dermal tests were positive to milk, egg yolk, meat, chicken and fish.

Treatment. On a diet eliminating these foods, the disappearance of her symptoms was striking. She gained weight, her bowel action became regular, and the attacks of diarrhea with mucus disappeared. The sigmoidoscopic examination was repeated one month after the diet was instituted and then the mucous membrane had a normal glistening appearance without any mucus adherent to it. It is now three years since the allergic foods were eliminated and during this entire period she has remained well. Several times she was told to include chicken or egg yolk in her diet, but each time she experienced abdominal pains several hours later.

CASE II.—Mrs. C. R., aged forty years, three children alive and well; occupation, helper in a fish store.

Family History. Father had asthma.

Past History. Negative.

Present History. For five years she had daily pains of a cramplike character in the midepigastrium, frequently radiating to the right hypochondrium without relation to meals; frequent pyrosis and nausea. The bowels were costive; she never observed whether mucus was present.

Physical Examination. This patient was of the asthenic type with moderate enteroptosis. On deep pressure there was tenderness in the epigastrium. The transverse and sigmoid portions of the colon were palpable, spastic and tender to pressure.

Technical Examinations. Gastric analysis revealed anacidity. On *sigmoidoscopic examination* the colon was found lacking in its normal glistening appearance and gray shreds of mucus were firmly adherent to the mucosa in small areas throughout the rectum and sigmoid.

Dermal tests were positive to the following sea foods: Pike, shad, cod, lobster and oyster. Reactions were also obtained to onion, tomato, veal, duck, raspberry, banana, lemon and cocoa.

Treatment. Dilute HCl after meals and colon irrigations failed to relieve her symptoms. As she worked in a fish store, sea foods constituted a large portion of her daily diet. After restriction of the foods to which

she proved sensitive her symptoms gradually disappeared, and after two weeks she felt well. Six weeks later the sigmoidoscopic examination was repeated, and the mucosa appeared normal. On several occasions she was instructed to eat of the sea foods mentioned but their ingestion always caused a return of her former symptoms. This patient has been under observation for the past two years and has remained well. Occasionally, because of her enteroptosis she still employs a colon irrigation when her bowels become constipated.

CASE III.—Mr. M. P., aged thirty-three years, two children alive and well, plumber by occupation.

Family History. Negative.

Past History. Negative.

Present History was four years in duration, and consisted of frequent pressure pains in the right lower quadrant and epigastrium soon after meals. His bowels were very constipated and moved only by enemata in which he frequently noticed strands of thick mucus. His appendix was removed two years after the onset of his symptoms but without relief. A Sippy treatment was also instituted for suspected duodenal ulcer but without success.

Physical examination revealed a well-developed man of sthenic habitus. There was distinct tenderness to pressure in the midepigastrium. The cecum, ascending colon and sigmoid were palpable and tender to deep pressure.

Technical Examinations. In the *sigmoidoscope* the mucosa of the rectum and sigmoid appeared glazed and congested with large areas covered by thick adherent brown mucus.

Dermal tests were positive to potato and garlic.

Treatment. After the omission of potato and garlic his symptoms rapidly disappeared and his bowels became regular. One month later the sigmoidoscopic examination revealed a normal mucosa. Thinking he was permanently cured he broke his diet a few days later and ate a large portion of potatoes. This was followed the same day by a recurrence of his former symptoms and the following day sigmoidoscopy revealed a recurrence of the picture of mucous colitis. As he was very fond of potatoes, oral desensitization was attempted. At the start he was found to tolerate one teaspoonful a day of mashed potatoes. Each week this was increased by an additional teaspoonful until now he can eat two potatoes a day without symptoms resulting.

CASE IV.—Mrs. E. M., aged fifty years, two children alive and well.

Family History. Mother suffered from asthma.

Past History. Negative.

Present History. For eight years she had constant burning sensations in the midepigastrium with shifting cramplike pains in both lower quadrants of the abdomen. These symptoms were increased several hours after meals. Her bowels were usually regular but occasionally there were attacks of diarrhea, with as many as ten movements a day, in which long strings of mucus were passed.

Physical Examination. This patient was a well-developed, sthenic type of woman. The colon was palpable, spastic and tender throughout its entire course, especially over the cecum and ascending colon.

Technical Examinations. Sigmoidoscopy revealed a dry congested mucosa with a marked excess of thick, adherent mucus in the rectum and sigmoid.

Dermal tests were positive to egg, cheese, herring, orange, prune, radish, celery and rhubarb.

Treatment. After avoiding these foods her condition returned to normal. After a symptom-free interval of one month she was instructed to include an orange and two eggs for breakfast which resulted in a reappearance of her

former pains the same day. These rapidly disappeared on resuming her diet, and she has remained well to the present time—a period of observation lasting one and a half years.

CASE V.—Miss M. N., aged twenty-five years, occupation, office worker.
Family History. Negative.
Past History. Negative.
Present History. For two years she experienced pressure pains in the midepigastrium occurring at irregular intervals and not related to meals. The bowels were frequently constipated and on several occasions she noticed an excessive amount of mucus in the stool. Three months after the onset of her gastric complaints she developed a generalized urticaria, which recurred every few weeks.
Physical examination revealed a well-developed young woman of sthenic habitus. There was tenderness to pressure in the midepigastrium. The cecum was palpable, spastic and tender.
Technical Examinations. The *sigmoidoscopic examination* showed a congested mucosa with thick strands of mucus adherent to it.
Dermal tests were positive to tomatoes, eggs, goose, pike and salmon.
Treatment. After omitting these foods her abdominal pains disappeared, her bowels became regular, and mucus was no longer observed. The sigmoidoscopic examination could not be repeated as she objected to it. Several times she forgetfully ate eggs or tomatoes, and each time she experienced a recurrence of her previous symptoms and urticaria. She has been under observation for one year, and is free from any abdominal symptoms or urticaria while on the restricted diet.

Conclusions. 1. Five cases are presented in which food allergy was the cause of mucous colitis.

2. The symptoms and objective findings disappeared following the withdrawal of foods to which the patients were sensitized, and could be made to reappear by their ingestion.

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THE DIAGNOSIS OF INTESTINAL OBSTRUCTION BY ROENTGEN-RAY.

BY WILLIAM K. KALBFLEISCH, M.D.
WHEELING, W. VA.

(From the Roentgen ray Department of the Wheeling Clinic, Wheeling, W. Va.)

IN 1901, Rudis-Jicinsky[1] successfully diagnosed by means of the Roentgen ray a case of intestinal obstruction caused by the swallowing of a foreign body which was opaque to the Roentgen rays. Therefore, he recommended that a patient suspected of having an

intestinal obstruction should be given an opaque pill by mouth in order that the progress of the pill through the intestinal tract might be observed under the fluoroscope; and, in that way, the location of the obstruction determined. The introduction of the contrast meal by Rieder and later the use of a barium suspension simplified this procedure.

If a definite diagnosis of intestinal obstruction can be made from the clinical picture, the surgeon, realizing the necessity of early intervention, will not feel that it is desirable to subject the patient to a Roentgen ray examination in order to obtain more exact information in regard to the location of the trouble. The surgeon would feel that the filling of the intestines with the heavy barium suspension and the length of time required for Roentgen ray examination would increase the operative risk out of proportion to the amount of benefit to be obtained from the additional information. However, there are certain cases in which the clinical picture is not absolutely clear and the indications for operation are not so urgent, in which the surgeon will welcome proof of the presence of the obstruction and information as to its possible location.

In 1922, A. C. Guillaume[2] made an interesting observation in connection with the Roentgen ray diagnosis of intestinal obstruction. In all such cases there is a distention of the intestines proximal to the obstruction by gas and fluid. He proved by a series of cases that these distended intestinal loops can be clearly demonstrated on a plain Roentgen ray film without the administration of a contrast meal. A picture which shows several of these distended intestinal loops may be considered pathognomonic of intestinal obstruction. Guillaume felt that the evidence offered by the plain film was so conclusive that he could entirely dispense with the use of the contrast medium.

The same observations were made by James T. Case[3] in 1923. He emphasized particularly the significance of the gaseous distention in the intestinal loops proximal to the obstruction. Case uses the plain picture routinely, but in cases of doubt administers ½ ounce of barium sulphate suspended in water as a contrast medium and under the fluoroscope observes the progress of the meal until it stops. For confirmation of the fluoroscopic findings he makes another examination five or six hours later.

In reading over the literature pertaining to this subject, I have found no mention of the position in which the patient should be placed for this examination. No doubt the prone position is used routinely, especially in dealing with very sick patients. Unfortunately, the most important observation cannot be made with the patient in the prone position. It is necessary for him to be in the upright position in order to demonstrate the presence of fluid levels in the intestinal loops, a phenomenon which I consider of the greatest significance.

In normal individuals, the amount of gas in the small intestines is minimal. After the barium meal has been administered, the three-hour picture shows the snowflake-like filling of the jejunum on the left side of the abdomen, and the sausage-like appearance of the loops of ileum lying in the true pelvis. In normal individuals, we never see a fluid level. The picture is entirely different in a case of intestinal obstruction. The intestinal loops are distended with gas and we readily recognize the fact in studying the flat film because the collections of gas offer less obstruction to the passage of the Roentgen rays than fluid or body tissue. If we place the patient in the upright position, the fluid in the intestinal loops will gravitate to the lowest parts and the gas will stand above it, thus forming horizontal fluid levels. Therefore, we can safely say that if we see distended loops of the small intestines with one or more distinct fluid levels, even in an unprepared patient, we can make the diagnosis of intestinal obstruction. Furthermore, we may be able to determine the location of the obstruction from the position of these loops, which are distended with fluid and gas. The author is of the opinion that we can dispense with a contrast medium in these cases, but the absolutely essential requirement is, that the patient be examined in the upright position.

For the illustration of this thesis, the following case history is presented. The case is remarkable from other standpoints as well as that of diagnosis.

Case Report. J. O'M., mill worker, aged twenty-nine years, white, single, came to the Wheeling Clinic, December 3, 1926, with the following history:

Present Illness. About Thanksgiving, he suddenly felt severe cramps in the left upper abdomen below the costal margin. The pains, sharp in character, gradually increased and at the time he was seen in the Clinic were felt all over the abdomen. They were present almost continuously from the onset of the illness. If he ate, he vomited at once, but he could drink water without being nauseated. December 2, he vomited bloody material. The stools were very light in color.

Previous History. He had measles and mumps in his childhood. His appendix was removed in 1916 and he had influenza in 1918. He further stated, that he was struck across the chest by a heavy iron bar four weeks previous to his present illness.

Family History. Essentially negative.

Physical Examination, December 3, 1926. The patient is a well-developed and well-nourished man about twenty-eight years of age. The expression of his face is somewhat anxious and he appears to be sick. No eruptions of the skin; no icterus. Pupils react sluggishly to light. External ocular movements are well executed. No strabismus. The ears are negative for mastoid tenderness, tophi and discharge. There is no impaction of cerumen. The tongue is

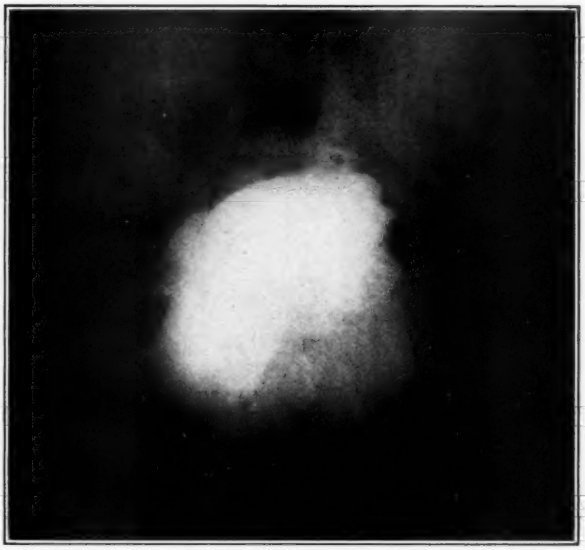

FIG. 1.

FIG. 2.

slightly coated, protruded in the median line without tremor. The teeth are only in fair condition, gums fairly firm. Pharynx negative, nothing expressed from either tonsil. There is no enlargement of the thyroid gland. There are no unusual pulsations, no tracheal tug, no bruit and no other abnormality noted in the neck. The nose is flattened by previous fracture. Axillary and inguinal glands palpable, also the epitrochlear glands on the left side. Skin and mucous membranes are normal in appearance. There is no enlargement of the heart in either direction. No palpable shock or thrill, no murmurs. Heart sounds are regular, clear and rhythmical. No adventitious sounds are heard. The lungs are negative by auscultation and percussion. The spine is straight, no deviations or deformities, no tenderness anywhere along the course of the spine. Fist percussion is negative over both kidneys. The extremities are negative. Knee jerks are active and equal on both sides, as are the Achilles tendon reflexes. There is no tremor of the hands with arms extended. The abdomen is normal in appearance except for a scar in the lower right quadrant. There is tenderness over the whole abdomen but especially below the left costal margin. No hernia is palpable, no masses felt, no enlargement of the liver or of the spleen. Neither kidney is palpable.

A provisional diagnosis of diaphragmatic hernia was made, and the patient was referred to the Roentgen ray department for an examination of the gastrointestinal tract.

Roentgen Ray Examination of the Gastrointestinal Tract. After filling the stomach with one glass full of barium-suspension mixture, we see a small hypertonic stomach, axis oblique, position in front of the spine. The pylorus is small and lying to the right of the spine. The duodenal bulb is small and lying behind the pylorus. The meal passes through the esophagus without hold-up. The patency of the cardia is intermittent. The fundus of the stomach fills first and shows in the lateral view a water-trap outline, the lower portion being pressed forward by gas-filled loops of the small intestines. After some time, the pyloric region of the stomach is also filled. The patency of the pylorus is intermittent. Peristalsis changes in intensity. The evacuation is early. The duodenum and the upper part of the jejunum fill up, but the meal does not proceed further. During the fluoroscopic examination the duodenum and first part of the jejunum appear dilated. The stomach itself is freely movable and not tender on palpation. The patient complains, however, of severe tendernesss just below the left costal arch. In this region, we see a well-filled intestinal loop with a horizontal fluid level, over which a collection of gas is noted. The barium has not as yet entered this part of the jejunum.

Two hours later there is about half of the meal left in the stomach. The whole duodenum is densely filled and distended. The intestinal loop with the fluid level, which was seen without a contrast medium

at the first examination, now shows barium filling. It is more expanded but shows the same fluid level with the gas bubble at the top. A few traces of barium may be seen in the lower parts of the small intestines.

Roentgen Ray Diagnosis: Partial obstruction in the upper part of the jejunum.

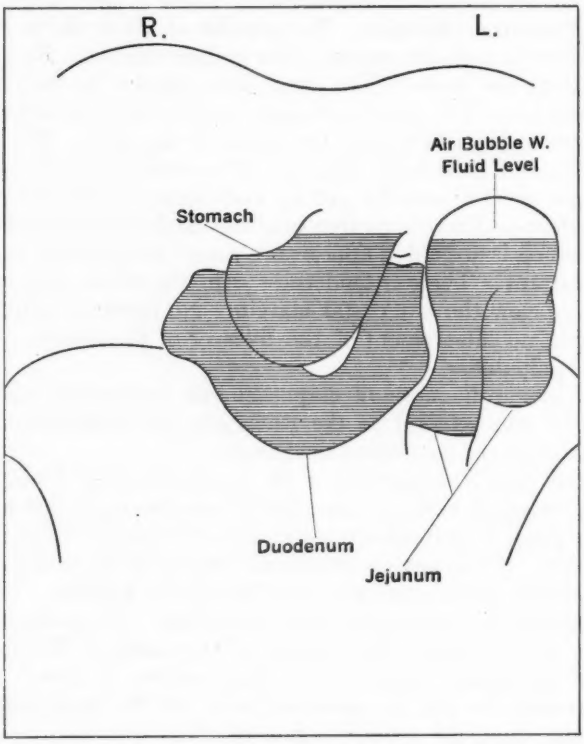

CHART I.—The diagnosis of intestinal obstruction by roentgen ray.

Operation (December 4, 1926). High rectus incision. The first 18 inches of the jejunum are markedly distended and the walls thickened. The jejunum at the end of this distention shows a napkin ring stricture about 1 inch in width, indurated and scarlet in color with almost no lumen palpable. There were two more indurated areas proximal to the one just described but not as extensive. The mesentery supplying the diseased portions of the jejunum is filled with great black bunches of glands, which extend up to the abdominal aorta. One gland was removed for examination, and anastomosis made between the upper jejunum and the jejunum distal to the ulceration, and the abdomen closed.

Pathologic Report. Microscopic examination shows the section of a lymphatic gland with a general thickening of the capsule and a marked lymphocytic infiltration. In the substance of the gland numerous very small miliary tubercles are seen. These consist for the most part of a centrally placed giant cell surrounded by concentrically arranged epithelioid cells. None of the tubercles have reached very large size and none of them show caseation.

Diagnosis. Tuberculosis of a mesenteric lymph node.

I am pleased to add that the patient had an uneventful recovery. The wound healed by first intention. After he was dismissed from the hospital, the patient had a series of Alpine-light treatments, in

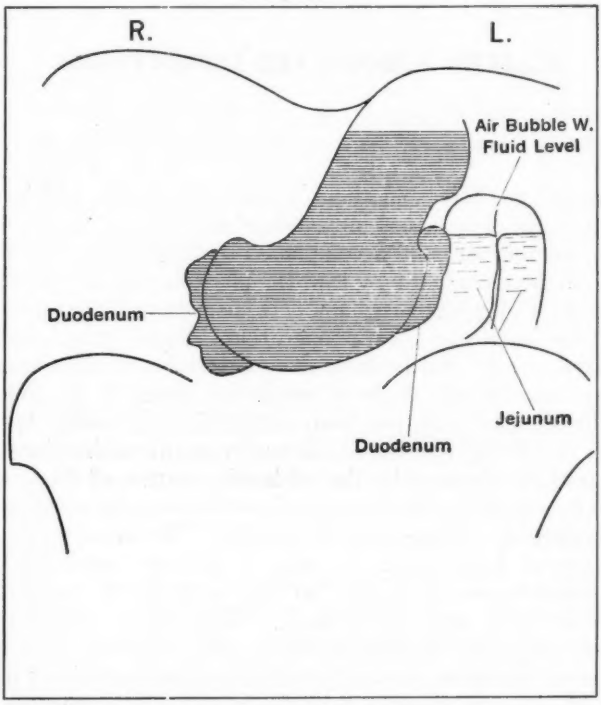

CHART II.—The diagnosis of intestinal obstruction by roentgen ray.

the course of which he gained more than 20 pounds in weight. When I saw him last, February 18, 1927, he felt absolutely well and had no clinical signs of an intestinal or peritoneal tuberculosis.

Conclusions. 1. Distended intestinal loops filled with gas and fluid are suggestive of intestinal obstruction.

2. The diagnosis is confirmed by the appearance of fluid levels in the intestinal loops.

3. This phenomenon can be demonstrated only if the patient is studied in the upright position, and we wish to emphasize the importance of this technique for the roentgenologic examination.

4. If the clinical picture suggests an intestinal obstruction the use of a contrast medium is unnecessary. The distended intestinal loops with demonstrable fluid levels are evidence enough.

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DIABETIC ACIDOSIS AND LEUKOCYTOSIS.

By Frank N. Allan, M.B. (Tor.).
FELLOW IN MEDICINE, THE MAYO FOUNDATION, ROCHESTER, MINN.

Diabetic acidosis sometimes causes symptoms which closely simulate those of an acute intraäbdominal lesion. Nausea, vomiting, and abdominal pain, accompanied by tenderness and apparent rigidity of the abdomen may lead the physician to suspect appendicitis, or other surgical emergency. It has been said that many cases of acidosis narrowly escape operation. Even when acidosis is recognized, it may still be difficult to determine whether the symptoms are due to the diabetic condition alone, or to concurrent abdominal disease; this has been emphasized by Joslin, Appel and Cooper, and Peters and his associates, in recent publications.

The confusion caused by the misleading nature of the symptoms may be increased by the leukocytosis which may be associated with acidosis entirely independent of infection. Emerson mentions the occurrence of leukocytosis in cases of diabetic coma, and Appel and Cooper comment briefly on the leukocytosis manifested in several of their cases of acidosis. With these exceptions, this phenomenon seems to have received scant attention in textbooks and current literature, probably because the association of infection with acidosis is so common that the increase in leukocytes is naturally attributed to the former.

Five cases of diabetic acidosis in which leukocytosis was found have been observed recently at the Mayo Clinic. I am reporting them in detail and the laboratory findings in tabular form.

Report of Cases. Case I.—A girl, aged nine years, had suffered from diabetes for twenty months, but the disease had been well controlled by careful regulation of diet and the use of insulin. Two weeks before admission she was taken ill with acute abdominal colicky pain accompanied by anorexia and nausea. The pain subsided in two days, but a few days later

returned and remained for twenty-four hours. Slight soreness and tenderness persisted in the lower part of the abdomen, especially on the right side. Her physician suspected appendicitis and sent her to the Mayo Clinic. Meals and insulin were taken as usual until she started on her journey, but glycosuria was not completely controlled. On the train the evening dose of insulin was omitted. During the ensuing night she wakened and vomited repeatedly. She felt pain in the back and later in the abdomen. In the morning she was weak and drowsy. When admitted to the hospital at noon she was almost comatose and breathing was deep and labored. She could be aroused but was unable to speak clearly.

Definite tenderness and rigidity of the abdomen were not elicited although examination was unsatisfactory on account of the hyperpnea. Considerable dehydration was shown by the dry tongue and skin. The physical condition was otherwise normal and roentgenogram of the chest was negative. The carbon dioxid combining power of the plasma was 12 per cent by volume, and the blood sugar 0.338 gm. per cent. The leukocytes numbered 66,400 at the first count, and 59,100 at the second count, with 90 per cent polymorphonuclear neutrophils. The temperature was 98°.

The child was obviously suffering from severe acidosis, yet the situation presented a difficult problem: the condition might have been precipitated by an exacerbation of appendicitis, which had perhaps been smoldering since the first pain two weeks previously, or acidosis alone might be responsible for the symptoms of this attack; immediate surgical intervention might be demanded, or operation might prove a needless hazard. It was thought improbable that leukocytosis of such degree would occur under these circumstances in the absence of infection. Since no sign of infection could be found elsewhere, it was natural, in view of the recent history, to suspect appendicitis. However, the increase in leukocytes was so great as to indicate that appendicitis, if present, had probably gone on to general peritonitis. For this reason, as well as on account of the uncertainty of diagnosis and the great risk entailed, operation was not advised. Acidosis was combated vigorously and developments awaited.

The following morning the patient seemed almost normal. The carbon dioxid combining power had risen to 30 per cent, and the leukocytes had fallen to 20,200. The next day they numbered 16,000 and a day later 10,100. Recovery was rapid and the child felt well in a few days. It was thought advisable to remove the appendix before sending the patient home. At operation two weeks after admission, there was macroscopic evidence of disease, and the pathologist reported chronic catarrhal appendicitis.

Comment. This case, characterized by unusually marked leukocytosis, illustrates the difficulty in diagnosis when an acute abdominal condition is suspected. Although appendicitis had probably been responsible for the earlier attacks of abdominal pain, the small amount of pathologic change found at operation does not justify attributing to acute appendicitis the condition at the time of admission to the hospital. It was finally concluded that acidosis was the result of omission of the usual dose of insulin, and the leukocytosis was considered a manifestation of acidosis. Although there might be some doubt in this with regard to the cause of the acidosis leukocytosis, the following cases, uncomplicated by infection, show that acidosis alone may be responsible for leukocytosis. The relative constancy of the hemoglobin and erythrocytes proved that the increase in leukocytes was not due to dehydration.

CASE II.—A married man, aged twenty-seven years, was admitted to hospital August 25, 1926, in a state of severe acidosis. He had suffered from diabetes for seven years. The diet had been restricted and during the last three years he had been using insulin, but without completely controlling the disease. He left his home to come to the Mayo Clinic on the morning of August 24, and while on the train did not take his usual dose of from 30 to 40 units of insulin a day. During the day he began to suffer from weakness, malaise, and abdominal pains. At 2.00 A.M. hyperpnea was manifested, and he arrived at the hospital at 10.00 A.M. on the verge of coma.

Respiration was of the typical Kussmaul type. The patient was lethargic, but not unconscious, and groaned constantly from pain in the chest. The urine contained large amounts of sugar and acetone bodies. The carbon dioxid combining power of the plasma was 8 per cent by volume. The leukocytes numbered 28,000. Insulin was given in repeated doses, 70 units being used in the first twelve hours, and the acidosis gradually disappeared. The leukocytes had fallen to 20,000 at 5.00 P.M., and the following day had become normal. Glycosuria was subsequently controlled by means of a diet with a total sugar value of 120 gm., and 15 units of insulin twice daily.

Comment. Acidosis in this case was the result of inadequate control of diabetes, and was precipitated by omission of the usual daily dosage of insulin during the railway journey.

CASE III.—A girl, aged fourteen years, began to have the symptoms of diabetes one month before admission. She complained of marked polyuria and polydypsia and her weight fell from 116 to 68 pounds. During the last week she had become extremely weak and drowsy, was short of breath on slight exertion, and suffered from a dull aching pain in the epigastrium. Diabetes was not recognized until the day before admission, when a physician was first consulted.

On admission the patient was in a state of exhaustion and quite stuporous. She could respond to questions, but afterward said she had no recollection of her entrance to the hospital. There was slight difficulty in breathing but no hyperpnea. The carbon dioxid combining power was 18 per cent. The leukocytes numbered 19,000.

Acidosis was quickly controlled with 50 units of insulin in the first twelve hours. The leukocytes fell to 13,800 on the day after admission, and on the following day reached normal.

Comment. The cause of acidosis was simply the rapid progress of severe juvenile diabetes, which had been unrecognized and untreated until coma had almost ensued.

CASE IV.—A married woman, aged forty years, had suffered from severe diabetes for more than five years. Since December, 1922, she had used insulin, and as a rule had good health although care of the diet was not always exact. In the summer of 1926 she began to complain of nervousness, insomnia and loss of strength. There was also abdominal discomfort after eating, and sometimes vomiting. On this account the diet and injections of insulin were irregular. August 23, she left home to come to the Mayo Clinic and, as she was unable to eat her usual meals, she unwisely omitted entirely her usual daily dose of from 40 to 60 units of insulin.

On the patient's admission to hospital at noon August 24, she was weak and slightly drowsy. The breath had a strong odor of acetone; the face

was flushed and the tongue dry. Urinalysis disclosed intense glycosuria and ketonuria. The carbon dioxid capacity of the plasma was 15 per cent; the blood sugar was 0.340 per cent. The leukocytes numbered 16,900.

During the next twelve hours 90 units of insulin were given, and the following morning the patient was feeling better. The carbon dioxid combining power had risen to 43 per cent, and the leukocytes had decreased to 11,500.

It was subsequently discovered that the patient was suffering from hyperfunctioning adenomatous goiter. Thyroidectomy was advised, and carried out September 4.

CASE V.—A girl, aged twenty years, had complained for two years of loss of weight and strength, nervousness, and palpitation. Three weeks before examination she had begun to suffer from thirst and excessive urination. The urine was not examined until the day before admission. Glycosuria was found and the patient immediately started on quite a long journey to the Mayo Clinic. While on the train she became extremely weak and during the night complained of nausea and vomiting. She was admitted to the hospital the following afternoon in a state of collapse. She was semicomatose but seemed restless and irritable. The respiratory rate was twenty-four and breathing was a little deeper than normal. The skin was dry and the tongue parched. Signs of exophthalmic goiter consisted of slight enlargement of the thyroid with bruits, prominence of the eyes, tachycardia, high pulse pressure, and trophic changes in the finger nails. The laboratory findings were as follows: Urinalysis showed sugar graded 4+ and diacetic acid graded 4+. Leukocytes numbered 17,000. The blood sugar was 0.376 per cent; the carbon dioxid combining power was 14 per cent.

Insulin and iodin (Lugol's solution) were administered simultaneously as advised by Boothby and Wilder in cases of diabetic acidosis associated with exophthalmic goiter. During the first twelve hours 80 units of insulin were injected, and 90 minims of Lugol's solution was given partly by mouth and partly by rectum. The following morning the patient's condition was much improved and with further treatment acidosis rapidly disappeared. The leukocytes decreased to 12,000 on the second day and to 6000 on the third day. As the hyperthyroidism subsided under treatment with Lugol's solution, the diabetes became comparatively mild, and two weeks after admission the patient could utilize a diet having a total sugar value of 150 gm. with only 10 units of insulin daily. Thyroidectomy was performed later.

Comment. In the last 2 cases, the development of acidosis was undoubtedly dependent on hyperthyroidism which exaggerated the intensity of the diabetes. In Case IV the omission of the usual injections of insulin was an additional factor.

Summary. Diabetic acidosis may simulate appendicitis not only in its clinical manifestations, but also in the occurrence of leukocytosis. A case is described in which association of appendicitis was strongly suspected, the leukocytes numbering more than 60,000. Other cases of acidosis are described to demonstrate the occurrence of leukocytosis in the absence of infection. In these cases the leukocytes varied from 16,000 to 28,000; return to normal rapidly followed the disappearance of acidosis.

ANALYSIS OF LABORATORY DATA.

Case.	Date and hour.	Hemoglobin, per cent.	Erythrocytes, millions.	Leukocytes.	Differential count.						Blood.		Urine.		
					Lymphocytes, per cent.	Large mononuclears, per cent.	Transitionals, per cent.	Neutrophils, per cent.	Eosinophils, per cent.	Basophils, per cent.	Sugar, per cent.	Carbon dioxid combining power of plasma, per cent.	Sugar.	Diacetic acid.	Insulin, units.
I.	May 31, 1926	..	..	..	..	..	..	..	..	..	..	..	..	..	80
	2.00 P.M.	..	..	66,400	..	..	..	..	..	..	0.338	12	4+	4+	
	5.00 P.M.	..	..	59,100	7.0	..	2.0	90.5	..	0.5	..	..	..	..	
	7.45 P.M.	..	..	..	..	..	..	..	..	..	..	16	4+	2+	
	June 1	..	..	20,200	..	..	..	..	..	..	0.117	30	0	0	35
	June 2	65	3.96	16,000	..	..	..	..	..	..	..	..	15.1 gm.	0	20
	June 3	..	..	10,100	..	..	..	..	..	..	..	..	37.1 gm.	0	25
II.	Aug. 25, 1926	..	..	..	..	..	..	..	..	..	..	..	..	..	60
	10.00 A.M.	82	5.08	28,000	18.5	..	1.0	80.0	..	0.5	0.390	8	4+	4+	
	4.00 P.M.	..	..	..	..	..	..	..	..	..	0.161	19			
	5.00 P.M.	..	..	20,000	23.0	0.5	3.0	73.5	..	..	..	..	4+	+	
	Aug. 26	..	..	9,300	30.0	..	3.6	65.5	1.0	0.5	..	..	23.3 gm.	0	50
	Aug. 27	84	4.96	9,200	27.0	2.0	..	70.0	1.0	..	0.236	53	20.2 gm.	0	55
III.	Sept. 25, 1926	..	..	..	..	..	..	..	..	..	..	..	..	..	50
	3.00 P.M.	85	4.78	19,000	41.0	1.0	3.0	55.0	..	..	..	18	4+	4+	
	5.00 P.M.	85	4.72	18,400	..	..	..	..	..	..	0.154	54	3+	4+	
	Sept. 26	85	5.00	13,800	25.0	1.0	2.0	72.0	..	..	0.094	53	6.0 gm.	0	30
	Sept. 27	84	4.96	9,200	27.0	2.0	..	70.0	1.0	..	..	..	39.0 gm.	0	50
IV.	Aug. 24, 1926	..	..	16,900	9.0	..	0.5	90.5	..	..	0.340	15	4+	4+	80
	Aug. 25	77	4.81	11,500	14.5	..	1.5	83.5	..	0.5	0.132	43	14.7 gm.	0	40
V.	Mar. 1, 1927	74	4.48	17,000	13.5	..	3.5	83.0	..	..	0.376	14	4+	4+	80
	Mar. 2	..	..	..	..	..	..	..	..	..	..	..	..	..	75
	8.00 A.M.	76	4.56	12,400	9.5	..	1.5	89.0	..	..	0.197	30	11.1 gm.	0	
	4.00 P.M.	75	4.52	12,000	23.0	2.5	6.0	67.5	..	..	0.115	41	Trace	0	
	Mar. 3	75	4.38	6,000	45.0	2.0	3.0	50.0	..	..	..	38	Trace	0	80
	Mar. 4	75	4.37	5,300	..	..	..	..	..	..	0.225	49	0	0	80

NOTE.—Since this article was submitted for publication an article by Joslin, Root and White,[7] with similar findings of leukocytosis and diabetic coma, has been published.

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MILK INJECTIONS: A STUDY OF BODY TEMPERATURE AND THE LEUKOCYTES.

By Frank H. Rodin, M.D.,

and

Rexford W. McBride, M.D.,

San Francisco, Calif.

(From the Department of Ophthalmology, Stanford University Medical School.)

Saxl[1] and Schmidt[2] introduced milk as a form of nonspecific protein therapy in 1916. Müller and Thanner[3] were the first to introduce its use in ophthalmology, where it has been used extensively. Since then, this form of therapy has been used in almost every branch of medicine and surgery. The bibliography of milk injections is voluminous. It has been used with varying degrees of success in children's diseases,[4] pelvic infections of women,[5] diseases of the skin and syphilis[6] including tabes and paralysis,[7] disturbances of the digestive apparatus and metabolism,[8] tuberculosis,[9] influenza[10] hemorrhage in typhoid as a hemostat,[11] asthma,[11] erysipelas,[12] arthritis,[13] urethritis and epididymitis,[14] ear infections,[15] for increasing the general resistance of patients before operations,[16] and septicemia.[17] It has also been used in veterinary medicine.[18]

A leukocytosis and an elevation of the temperature were noted by almost all observers. Gellhorn[5] who had treated many pelvic infections by milk injections reported that in the majority of cases the temperature rose to between 100° and 102° F. and may rise as high as 105° F. He used ordinary whole milk sterilized for ten minutes in a waterbath or pasteurized at 80° C. for one hour on six successive days. Starting with 5 cc. he gradually increased the dose to 10 cc. Shorney[19] obtained a temperature from 101° to 102° F. and in one patient it rose to 104° F. The milk, without incubation, was boiled from five to eight hours, and 15 cc. were injected. Bargy,[20] who had used injections of milk in 3000 patients, with an average dose of 5 cc., found the temperature to fluctuate around 38° C. (100.4° F.) and seldom reached 40° to 41° C. (104° to 105.6° F.). On securing the milk, he boiled it for ten minutes, and again for a few minutes before an injection.

Spektorovskaja,[21] using 2 cc. of sterilized milk, and studying the blood after injections in 22 patients with various illnesses and one healthy student, found in the majority of cases an hour after the injection of this small amount a moderate leukopenia with a decrease in the leukocytes from 700 to 1500. In a few of the cases the number of the white cells did not change. On the next day, however, a diminution in the leukocytes appeared and reached its

maximum on the second or third day. This decrease was from 2000 to 4000 leukocytes, averaging 2600. From that time on the leukocytes increased and reached their original number on the fifth or sixth day. In the remaining 20 per cent, a leukocytosis was observed, of which 2 cases showed a leukopenia for a short time. The increase in the leukocytes was from 1500 to 2500, and in only 1 case did it reach 7500. On the fifth or sixth day the number of white cells returned to normal. The temperature increased in 50 per cent, and did not go above 37.8° C. (100.2° F.).

Øwre[22] reported the changes observed in the blood after intramuscular injections of 5 cc. of milk in 6 healthy young adults. The temperature rose slightly in all, reaching 39.4° C. (102.8° F.) in one, and the leukocytes increased 2 or 3 fold.

Technique. This is a study of the temperature and leukocytes in 26 patients who received milk injections, using the same technique and dose. Both certified and pasteurized milk were used. The certified milk was obtained from one dairy and averaged 2900 colonies of bacteria per cubic centimeters, and the pasteurized from two sources averaging 200 and 3500 colonies per cubic centimeter. The source of supply played no part in the results obtained. Barkan and Nelson[23] have shown experimentally that for protein therapy milk of a high bacterial count should be used. This was obtained in our study by incubation: placing the milk in a sterile container, or in the original milk bottle, 8 inches from a warm radiator for six to twelve hours. No bacterial count of the incubated milk was made. The milk was then boiled for three minutes, according to the Vienna method.[21] This boiling time was chosen as being long enough to destroy the bacterial contamination and not long enough to inactivate whatever might be the active component contained in the milk. The injections were made deeply in the fleshy part of the buttocks with a 2½ inch needle, under the usual aseptic precautions. Fifteen cubic centimeters of milk were injected, except in a few cases when the injection consisted of 10 cc. Where the treatment was repeated, it was done in forty-eight hours and again in forty-eight hours. The leukocyte count and the differential was made from six hours to a few minutes before the injection, and again from six to twelve hours after the injection. The blood count was repeated every twenty-four hours for two to four days. In the differential leukocyte count, only the percentage of the polymorphonuclears and the lymphocytes are noted, as the other types of white cells showed no important changes. The blood counts were done by one of us (McBride).

The temperature was taken every two hours for three to five days. The pulse rate played no important part in this study and is therefore not recorded in the report. Other than a chill of various degrees observed in some patients, and a feeling of nausea and fever

developed by a number of others, no ill effects from the injections were noted.

Report of Cases.—Two cases are reported in full:

CASE I.—Acute iridocyclitis, dental origin. February 15, 1926, M. G., female, aged forty-six years, had had pain in the left eye for four days. The eye was tender to touch. Examination of the left eye showed a contracted pupil; swollen iris. The pupil dilated to maximum under atropin and dionin. The next day the iris was still discolored, the eye tender and injected. The leukocyte count was 9400; polymorphonuclears, 69 per cent; lymphocytes, 30 per cent. Fifteen cubic centimeters of milk were injected. The patient had a chill during the night. Four hours after the injection the temperature was 99.2° F. and four hours after that 100.4° F. Eleven hours after the injection the temperature was 102.4° F. The next day the temperature varied from 99.8° to 100.8° F. The leukocyte count was 14,800; polymorphonuclears, 80 per cent; lymphocytes, 20 per cent. The eye was improving.

February 18, the temperature at noon was 99.8° F. Ten cubic centimeters of milk were injected. The temperature remained 99.8° F. during the day. The leukocyte count was 15,600; polymorphonuclears, 84 per cent; lymphocytes, 16 per cent. The patient had a slight chill. The next day the temperature varied from 98.8° to 99° F. The eye was much better. A roentgenogram showed a large number of abscessed and dead teeth. The Wassermann reaction was negative. March 15, the eye was completely cured.

CASE II.—Acute iridocyclitis, rheumatic. January 21, 1916, N. H., male, aged fifty years, had had rheumatic fever one year previously. He was confined to bed for three months with swollen joints. For the last nine months the left eye had been painful and red at times. The vision was: right, 15/20; left, 15/100. Examination showed puffy, painful hands; intense bulbar injection of the left eye; ciliary injection; marked discoloration of the iris; tender eyeball; pupil 3 mm. in diameter with no reaction to light.

The eye was treated with instillations of atropin and subconjunctival injection of atropin and epinephrin.[24] The leukocyte count was 5900; polymorphonuclears, 25 per cent; lymphocytes, 73 per cent. Fifteen cubic centimeters of milk were injected. The next day the temperature rose to 101.6° F. The leukocyte count was 12,600; polymorphonuclears, 74 per cent; lymphocytes, 26 per cent. The following day the temperature was normal. The leukocyte count was 9300; polymorphonuclears, 36 per cent; lymphocytes, 61 per cent. The next day 15 cc. of milk were injected. Two and a half hours later the temperature was 100.2° F. The following day the temperature varied from 99.8° to 103° F. The leukocyte count was 12,200; polymorphonuclears, 62 per cent; lymphocytes, 38 per cent. The next day the temperature varied from 99.6° to 100.4° F. There was a gradual improvement in the eye condition.

Six weeks later there was a complete recovery with vision of the left eye 15/15. The patient claimed that since he had received the milk injections the pain and puffiness of the hands had also cleared up. The Wassermann reaction was negative.

Table I gives a summary of the cases. There were 26 patients: males, 18; females, 8. The youngest was aged nineteen years, and the oldest seventy-six years; the average age was forty-four and five-tenth years.

TABLE I.—SUMMARY OF CASES

Case.	Age.	Sex.	Diagnosis.	Number of injections given.	Maximum temperature.		Leukocyte count, maximum.		Polymorphonuclears.				Lymphocytes.				Comment.
									Before injection.		After injection.		Before injection.		After injection.		
					Before injection.	After injection.	Before injection.	After injection.	Per cent.	Number of cells.	Per cent.	Number of cells.	Per cent.	Number of cells.	Per cent.	Number of cells.	
1	46	F.	Acute iridocyclitis, dental origin	2	98.6	102.4	9.4	15.6	69	6.4	84	13.1	30	2.8	16	2.2	Marked improvement.
2	50	M.	Acute iridocyclitis, rheumatic	2	98.6	103.0	5.9	12.6	25	1.4	74	4.4	73	9.2	26	3.3	Marked improvement.
3	39	F.	Acute iridocyclitis, corneal ulcer, etiology undetermined	2	99.4	101.0	10.8	14.2	60	6.4	83	11.8	35	3.8	15	2.1	Some improvement.
4	76	M.	Acute iridocyclitis, glaucoma, subluxation of lens	2	98.6	98.6	11.6	17.3	68	8.0	80	13.9	27	3.1	16	2.8	Temporary improvement.
5	27	M.	Acute iridocyclitis, corneal involvement, syphilitic	2	98.6	102.0	12.6	17.6	80	10.1	82	14.4	18	2.3	18	3.2	No improvement.
6	40	M.	Acute iridocyclitis, etiology undetermined	1	98.6	100.0	7.5	17.5	54	4.0	80	14.0	45	3.4	20	3.5	Marked improvement.
7	55	F.	Acute iridocyclitis, syphilitic	2	98.6	103.4	7.2	15.4	61	4.4	70	10.8	34	2.4	30	4.6	Some improvement.
8	31	M.	Acute iridocyclitis, old interstitial keratitis.	2	98.6	100.4	7.1	13.5	61	4.4	80	10.8	30	2.1	20	2.7	Marked improvement.
9	33	M.	Acute iridocyclitis, syphilitic	1	99.2	102.0	9.1	15.0	69	7.3	85	12.7	28	2.5	15	2.2	Marked improvement.
10	36	M.	Acute recurrent iridocyclitis, etiology undetermined	2	98.6	100.8	6.8	10.4	54	3.7	68	7.1	43	2.9	28	2.9	Some improvement.

11	35	M.	Acute iridocyclitis, traumatic, positive Wassermann reaction	2	98.6	101.4	7.7	12.9	66	5.1	75	9.7	34	2.6	24	3.1	Marked improvement.
12	36	M.	Acute iridocyclitis, etiology infected tonsils (?)	1	98.6	99.0	9.0	14.5	64	5.8	81	11.7	32	2.9	19	2.8	Marked improvement.
13	50	F.	Acute iridocyclitis, dental origin	2	99.6	103.0	5.6	12.6	60	3.4	74	9.3	38	2.1	24	3.0	Marked improvement.
14	45	F.	Acute iridocyclitis, increased tension, dental origin (?)	1	99.6	100.0	12.0	17.4	70	8.4	82	14.3	25	3.0	18	3.1	Marked improvement.
15	70	M.	Postoperative iridocyclitis, positive Wassermann reaction	2	98.6	99.6	9.5	11.0	53	5.0	70	7.7	46	4.4	28	3.0	Marked improvement.
16	54	M.	Postoperative iridocyclitis	3	98.6	100.2	10.9	12.7	77	8.4	77	9.8	22	2.4	22	2.8	Some improvement.
17	70	M.	Postoperative iridocyclitis	3	98.6	100.6	7.1	13.6	64	4.5	79	10.7	35	2.5	16	2.2	No improvement.
18	60	F.	Postoperative iridocyclitis	1	98.6	100.4	10.0	12.8	71	7.1	84	10.7	25	2.5	16	2.0	Marked improvement.
19	53	M.	Kerato-iridocyclitis, neuroparalytic	2	98.6	101.2	8.2	15.7	66	5.4	80	12.6	34	2.9	18	2.8	Slight improvement.
20	34	M.	Recurrent chronic iridocyclitis, rheumatic	1	98.6	101.0	10.0	15.7	67	6.7	77	12.1	30	3.0	22	3.4	No improvement.
21	22	M.	Chronic iridocyclitis, syphilitic	2	98.6	102.0	11.4	15.3	69	7.9	79	12.1	28	3.2	15	2.3	No improvement.
22	41	M.	Corneal ulcer, endophthalmitis, syphilitic	1	99.0	99.4	10.4	13.8	66	6.9	79	10.9	31	3.2	18	2.5	No improvement.
23	19	F.	Pelvic peritonitis, gonorrheal	4	103.6	102.0	12.4	12.5	90	11.1	83	10.4	10	1.2	17	2.1	Marked improvement.
24	20	F.	Acute arthritis, gonorrheal	2	100.2	103.8	10.0	9.8	74	7.4	76	7.5	25	2.5	24	2.4	Some improvement.
25	57	M.	Acute arthritis, gonorrheal (?)	3	99.4	100.4	7.6	15.2	62	4.7	78	11.9	34	2.6	20	3.0	No improvement.
26	59	M.	Osteoarthritis	2	98.6	99.0	8.7	10.9	66	5.7	65	7.0	32	2.8	32	3.5	No improvement.
			Average for all cases	2	99.0	101.0	9.2	14.1	65	6.1	78	10.8	32.5	3.0	20.7	2.8	

All leukocyte figures are expressed in terms of thousands per cubic millimeter.

The diagnoses of the cases were:

Acute iridocyclitis	14
Acute iridocyclitis, postoperative	4
Chronic iridocyclitis	2
Kerato-iridocyclitis, neuroparalytic	1
Corneal ulcer, endophthalmitis	1
Pelvic peritonitis	1
Acute arthritis	2
Osteoarthritis	1

Fifty injections were given in all. One injection only, to 6 patients; 2 injections to 15; 3 injections to 3; and 4 injections to 1.

Temperature. The temperature obtained before the injection is given and also the maximum temperature after the injections. Only one patient, Case IV, who had a normal temperature before the injection failed to show an increase afterward. In Case XXIII, the highest temperature before the injection was 103.6° F. and after the injection the highest obtained was 102° F. Seven other patients who had a fever before the injections showed a further elevation of temperature afterward.

The elevation of temperature varied from 99° to 103.8° F. The highest elevation of temperature obtained in a patient with a normal temperature before the injection was 103.4° F. (Case VII). The average elevation of temperature was 2° F.

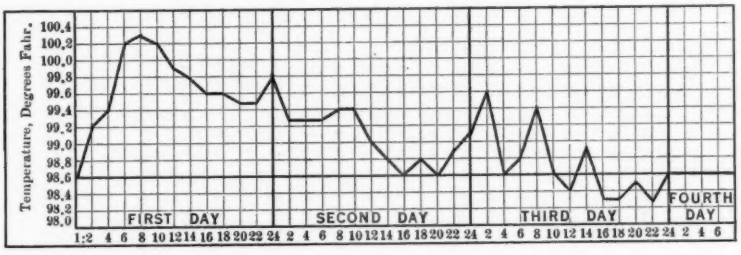

CHART I.—Composite temperature curve following 47 milk injections in 35 cases. Only such patients are included who had a normal temperature before the injection.

Chart I shows a composite temperature curve following 47 injections in 35 cases. Only such patients were included who had a normal temperature before the injection. There was a gradual elevation in temperature soon after the injection reaching the maximum, 100.3° F., in eight hours. This was followed by a slow fall and became normal forty hours after the injection. Then, the temperature again showed a slight elevation until sixty-four hours after the injection when it became subnormal (98.3° F.) and returned to normal on the fourth day.

It is interesting to compare this curve with the one obtained by Scully[25] using intravenous injections of typhoid vaccine in acute articular rheumatism. Giving 47 injections in 25 cases, there was a

gradual rise in temperature reaching 103.8° F. four hours after the injection, after which there was a gradual fall to nearly normal in sixteen hours and to normal in forty-eight hours. The curve obtained by Scully corresponds to that of Culver[26] who used: 54 gonococcus vaccine injections in 14 patients, 23 meningococcus vaccine injections in 12 patients and 8 colon bacillus in 7 patients.

Leukocytes. Table I shows the leukocyte count before the injection and also the maximum obtained after the injection with the percentage of polymorphonuclears and lymphocytes, and the absolute number of these cells. Twenty-four patients showed a leukocytosis after the injections, and of these 21 showed an increase in the percentage of polymorphonuclears and a decrease of the lymphocytes, while in 3 patients (Cases V, XVI, XXVI) the differential count did not change. Two patients, who already had a leukocytosis, did not show an increase in the leukocytes after injections (Cases XXIII and XXIV).

The increase in leukocytes in all cases varied from 16 per cent (Case XVI) to 132 per cent (Case VI). The average increase in the white cells was 4882, or 53 per cent. The increase in the percentage of the polymorphonuclears varied from no increase (Cases V, XVI, and XXVI) to an increase of from 25 to 74 per cent (Case II). The average increase was 13 cells per 100 counted, or 4679 polymorphonuclears. The average decrease in the lymphocytes was 11.8 cells per 100 counted, or 181 lymphocytes. A leukocytosis is obtained soon after the injection and persists from three to five days.

The improvement obtained was: marked in 12 patients; some in 5; slight in 1; temporary in 1; none in 7.

There is no uniform reaction to the injections even if the same milk is given to different patients, as is illustrated by Cases I and XVII (see Table II).

TABLE II.—EFFECT OF INJECTIONS OF THE SAME MILK TO TWO DIFFERENT PATIENTS.

Case.	Before injection.				After injection.			
	Temp.	W.B.C.	Polys. %	Lys. %	Temp.	W.B.C.	Polys. %	Lys. %
1	98.6	9.4	69	30	102.4	14.8	80	20
17	98.6	7.1	64	35	99.8	13.6	79	16

Two other patients, Cases XIII and XXI, first received injections of certified milk which was not incubated, and came from different bottles. Later, milk from a single bottle and incubated in the usual way was injected. More marked results followed the injection of the incubated milk (see Table III).

TABLE III.—EFFECT OF INJECTIONS OF NONINCUBATED MILK AND INCUBATED MILK (EFFECT OF INJECTIONS OF THE SAME MILK, INCUBATED, TO TWO DIFFERENT PATIENTS).

Case.	Before injection.				After injection. Non-incubated milk.				2 days later.				After injection. Incubated milk.			
	Temp.	W.B.C	Polys. %	Lys. %	Temp.	W.B.C	Polys. %	Lys. %	Temp.	W.B.C	Polys. %	Lys. %	Temp.	W.B.C	Polys. %	Lys. %
13	99.6	5.6	60	38	101.0	11.1	66	33	99.2	9.2	55	42	103.0	12.6	74	24
										(1 day later)						
21	98.6	11.4	69	28	100.2	15.3	79	15	98.6	14.4	65	28	102.0	12.4	80	20

Summary. 1. Of 26 patients receiving 50 milk injections, only 1 patient who had a normal temperature before an injection failed to show an elevation afterward. The average increase of temperature was 2° F.

2. Twenty-four patients showed a leukocytosis, and of these 21 showed an increase in the polymorphonuclears and a decrease in the lymphocytes. The average increase in the leukocytes was 4882, or 53 per cent. The average increase in the polymorphonuclears was 13 cells per 100 counted, or 4679. The average decrease in the lymphocytes was 11.8 cells per 100 counted, or 181.

3. The elevation of the temperature and the increase in the leukocytes and the percentage of the polymorphonuclears roughly parallel each other.

4. A study of the temperature and the leukocytes in milk injection offers an index to the therapeutic action of the milk.

Conclusions. In the cases studied only 1 patient, who had a normal temperature before the injection, failed to show an elevation afterward, and of the 26 cases only 2 patients, who already had a leukocytosis, did not show an increase in the white blood cells. While in some cases the degree of leukocytosis and elevation of temperature did not seem to have any bearing on the results obtained, however, our impression is, that cases with a marked elevation of temperature and a corresponding increase in the leukocytes and the percentage of the polymorphonuclears appear to give the best response to treatment.

The persistence of the temperature for about sixty hours and the leukocytosis from three to five days added to the fact that the reactions to milk injections are very mild as compared with other kinds of nonspecific protein therapy, justifies the use of milk for such treatment. In addition to that, milk is easily procurable at all times and everywhere, cheap, and easily prepared for treatment. In small doses it may be used for ambulatory treatment. For repeated injections it should be given every third or fourth day.

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FURTHER OBSERVATIONS WITH THE DIET RICH IN LIVER FOR THE TREATMENT OF PERNICIOUS ANEMIA.

By John Huston, M.A., M.D.,
ANN ARBOR, MICH.

(From the Department of Internal Medicine, University of Michigan Medical School, Ann Arbor, Mich.)

Since the publication of Minot and Murphy's article[1] concerning the use of a diet rich in liver for the treatment of pernicious anemia, we have observed a series of 30 cases on the same régime. The results obtained corroborate their observations in practically every respect. Of the 30 cases, 29 developed definite remissions while under observation. It is questionable whether the other case (No. 6) should be classified as a failure. She did not like the diet and her anemia was overshadowed by very advanced combined sclerosis. After one month's observation there had been very little change in either condition. Six weeks later she was feeling improved, but she did not return for further examination, which makes a final decision impossible.

With one exception (Case No. 30) the patients were hospitalized for an average period of one month because the majority found it difficult or impossible to return to the out-patient department for frequent observations. When it became evident that a remission was developing, further convalescence and treatment were continued at home. After an average interval of two months, 17 of the 22 patients who had been away that long returned for a check-up examination. From the 5 not returning communications were received indicating further improvement after discharge.

Dietary Management. The dietary management used has been essentially that described by Minot and Murphy.[1, 2] It has been very satisfactory in most cases, and coöperation was obtained with very few exceptions. The liver seems to be the essential element, and this was emphasized to the patients. Personal idiosyncrasies were frequent and were allowed for with respect to the other elements of the diet when good reasons were evident. Quite a few complained about the restriction of fat. In a few cases the allowance of 70 gm. was exceeded without detrimental effects. When improvement once developed, further trouble usually was not encountered. The increase in appetite usually was sufficient to take care of the food allowance and often more. In 3 cases the general condition on admission was so poor that transfusion was indicated. One case received two transfusions before she had sufficient strength to coöperate and eat the diet. All of these patients developed satisfactory remissions. Most of the patients received hydrochloric acid, but a few did not and they improved just as well as the others.

Changes in Physical Appearance. Subjective improvement is noted by the patients within a few days. They begin to feel better, are more cheerful, the appetite improves, and a progressive increase in strength is noted. All these changes progress rapidly, so that by the end of one to one and a half months they feel relatively well as far as ordinary activity is concerned. An improvement in color is usually very evident, and with the loss of the icteric pallor, approaches normal. This increase in redness of the face, lips, and so forth, is often deceiving, for it may be associated with blood findings which are as yet far below normal. An improvement in the condition of the mouth is universal. The improvement in circulation is readily discerned in the appearance of the tongue, but cases having true atrophy of the tongue show no improvement in this respect. Relief of previous gastrointestinal disturbances is relatively common. Diarrhea developed in several cases when first placed on the diet, but it subsided in every case without permanent ill effects.

NUMERICAL CHANGES IN THE BLOOD.

				Entry.		Discharge.		Return visit.	
Case	Duration, years.	Age.	Remissions.	% Hgb. Sahli.	R. b. c.	% Hgb. Sahli.	R. b. c.	% Hgb. Sahli.	R. b. c.
1	½	58	0	30	1,480,000	60	3,350,000	85	5,100,000
2	1	54	1	20	800,000	65	3,250,000		
3	2	42	0	25	950,000	65	3,000,000	75	3,600,000
4	3	62	1	30	1,400,000	70	4,000,000	85	3,900,000
5	2	45	1	25	950,000	70	3,450,000	85	4,300,000
6	1	62	0	70	2,900,000	70	3,600,000		
7	4	42	2	20	1,400,000	50	3,000,000		
8	1	60	1	60	2,500,000	70	3,000,000	95	4,500,000
9	1	50	0	20	860,000	50	2,500,000		
10	3	68	?	45	1,600,000	70	4,100,000		
11	1½	56	1	25	1,250,000	60	1,900,000		
12	1	57	1	25	1,000,000	70	2,670,000	90	3,600,000
13	2	40	2	20	1,200,000	50	2,900,000	90	4,000,000
14	2	44	2	20	1,000,000	65	2,900,000	65	3,500,000
15	2	34	?	35	1,600,000	70	3,600,000	85	4,200,000
16	2	50	1	20	1,000,000	70	3,900,000		
17	1	35	1	30	1,500,000	65	3,300,000		
18	8	62	3	20	920,000	70	4,100,000	85	4,500,000
19	1	50	0	35	1,800,000	60	2,200,000		
20	1	31	0	25	850,000	70	3,400,000		
Second entry				30	1,500,000	70	4,100,000		
21	1	60	0	30	1,000,000	75	3,000,000		
22	1	66	0	25	1,280,000	50	2,000,000	70	3,500,000
23	1	60	?	30	1,100,000	65	2,750,000	75	3,800,000
24	1	25	0	20	850,000	45	2,200,000	80	4,000,000
25	3	45	1	30	1,800,000	90	3,500,000	80	3,900,000
26	1	32	0	45	2,900,000	70	3,700,000		
27	1	34	1	50	1,600,000	65	2,300,000		
28	1	53	?	70	2,450,000	80	3,300,000	85	4,300,000
29	1	41	0	50	2,960,000	70	3,500,000	95	4,900,000
30	1	34	0	25	1,200,000	..	.....	90	4,750,000
Average				35−	1,480,000−	65+	3,250,000+	85−	4,150,000−

Changes in the Blood. Numerical changes in the blood were usually evident after the first week. The rapidity with which improvement developed and progressed was, however, quite vari-

able. No definite relationship between the patient's age, duration of the disease and number of previous remissions was evident. A summary of the numerical changes is given in table. As this table shows, most of the cases had had only one or no previous remission. Yet one of the most striking remissions occurred in (Case No. 18) a man aged sixty-two years, with three previous remissions and a duration of eight years. The average case on admission had hemoglobin, 35 per cent; red blood cells, 1,480,000; after an average period of one month hemoglobin, 65 + per cent; red blood cells, 3,250,000; after another average interval of two months, hemoglobin, 85 per cent; red blood cells, 4,150,000. Of the whole group only 1 case did not improve after discharge (Case No. 20) and this was definitely due to failure to follow the diet. After another period of management, she improved very satisfactorily.

The observed changes in the cells have been very much the same as Murphy and his coworkers[3] have described. Evidence of increased regeneration is observed within three to four days in most cases. The reticulated cells show an increase at this time which rises rapidly to reach an average maximum of 12 per cent at the tenth to fourteenth day. From this time the percentage decreases gradually reaching normal about the third to fourth week. Subsequently the percentage is very low and very frequently, at the return visit counts were less than 0.10 per cent. Normoblasts, stippled and polychromatophylic red cells appear or become increased with the rise in reticulated cells and diminish at about the same time. The changes in mean diameter of the red cells described by Medearis and Minot[4] are very definite with the development of a remission.

The decrease in blood destruction becomes evident about the first week. The onset of the decrease in blood bilirubin frequently coincides with the period of maximum production of the reticulated cells. The blood bilirubin usually reaches normal limits after a period of three to four weeks. Determinations at the subsequent visits were always within normal limits. The changes in red blood cells, reticulated cells, and blood bilirubin in a typical case are illustrated in Chart I.

Changes Noted at the Return Examination. Patients returning after an average interval of two months usually show a striking improvement in general appearance, which has little to suggest pernicious anemia. A gain in weight is the rule. The degree of redness of cheeks, and so forth, shown by same cases almost suggested an erythremia, but in no case was this found to be true, and quite frequently the high color was associated with blood findings which were distinctly below normal. Most of the patients, especially those without serious neurologic changes, have felt well enough to resume a part of their former activities. However, even in the

presence of a numerically normal blood a distinct decrease in reserve strength seems to exist which makes a lower level of activity advisable.

Blood-pressure observations revealed a tendency to higher levels. The average before treatment was systolic, 110; diastolic, 60; while at this return examination it was systolic, 130; diastolic, 85. Routine stool examinations were essentially negative. Gastric analyses showed a persistence of the achlorhydria. A summary of the blood findings is given in table, and shows that the improvement continues for several months after the diet is instituted. In addition to the changes in red blood cells and hemoglobin, the white count increased from an average of 3200 before treatment to 5100 at this time.

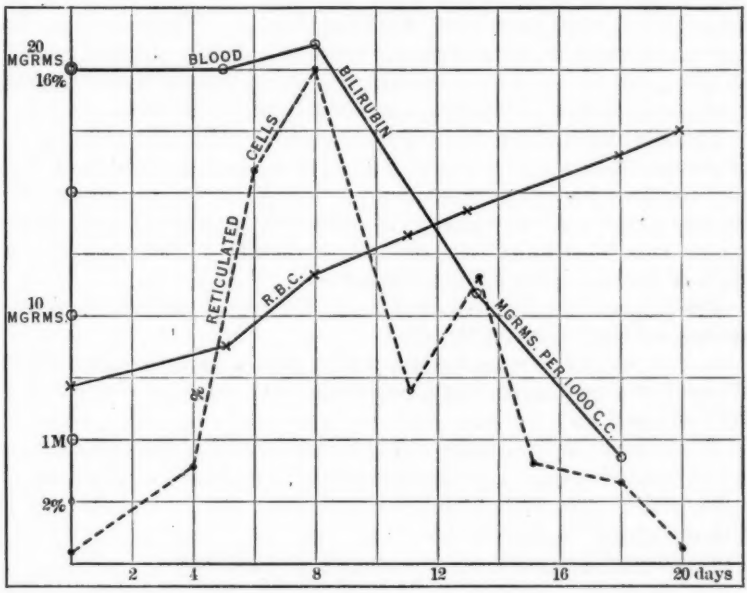

CHART I.

Aside from routine urine examinations, blood pressure and cardiovascular observations, no studies of the renal status were made in these cases because none of them had urinary abnormalities while under observation here. It seemed advisable, however, to observe the urine after this period of dietary management in view of the relatively high-protein content of the diet and because of the renal changes observed in some cases of pernicious anemia and in patients at the age at which the disease occurs. Two of the 17 cases observed had urinary findings which were distinctly abnormal compared with what they had previously shown. Case No. 22 had a very slight

trace of albumin, with a few hyalin casts. Case No. 23 developed edema of the feet and ankles after discharge, which had persisted. His cardiac condition was satisfactory. His urine showed a trace of albumin, with numerous hyalin and fine granular casts. Both patients have been seen too recently to observe the general trend of events, but the amount of liver was reduced to 100 gm. daily. One case, not observed in the Clinic, has come to our attention. A patient with a severe anemia was advised to eat a diet with a liberal allowance of liver, without considering the underlying chronic nephritis. Generalized edema, with other changes, developed, which led the family physician to believe the condition was an acute exacerbation of the chronic nephritis. The patient died. While other factors may have been partly or wholly responsible for the unfortunate course of events, yet the burden of the high-protein intake may have been a contributing factor. Whatever may be the explanation of these changes, there is a certain amount of risk in the unsupervised use of this diet by individuals without medical training or without consideration of the type of anemia.

Further observations on the cases are being made, but the number of patients observed for more than a few months is so limited that any conclusions as to the ultimate course of events are impossible. To our knowledge no relapses have occurred except in Case No. 20, which can be definitely attributed to dietary indiscretion in the light of her subsequent improvement.

Conclusions. 1. Twenty-nine out of 30 cases of pernicious anemia developed remissions on this diet.

2. The remission persists for a period of time as yet undetermined if the diet is continued, but a relapse is to be expected if the diet is discontinued for very long.

3. Evidence of bone-marrow regeneration is given by the increase in reticulated, stippled, polychromatophylic and nucleated red blood cells, and of decreased blood destruction by the progressive fall in the amount of blood bilirubin.

4. The achlorhydria persists during the remission.

5. The renal status should be considered in both the primary and secondary anemias when placed upon this diet.

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NITROHYDROCHLORIC ACID IN THE TREATMENT OF HAY FEVER.

By Harry Beckman, M.D.,

PROFESSOR OF PHARMACOLOGY AND MATERIA MEDICA, MARQUETTE UNIVERSITY SCHOOL OF MEDICINE, MILWAUKEE, WIS.

Anyone who would offer a new remedy for hay fever at this time must needs be bold indeed. It is, therefore, with no little trepidation that I invite the attention of the profession to nitrohydrochloric acid. My reason for urging the claims of the drug are the following: (1) 100 per cent of symptomatic cures in 17 cases treated during the past eight years; (2) the drug was suggested many years ago and very favorably reported upon by private practitioners, but no clinical studies of it on a large scale have ever been made; (3) the hope of stimulating such studies; (4) the considerable failure of the pollen-desensitization method of treatment.

Experience with the Drug. In 1918, Speidel[1] called my attention to the fact that Gleason[2] mentions the *oral* use of nitrohydrochloric acid in the seasonal treatment of hay fever. I had been a severe sufferer from the malady for many years, obtaining practically no relief from the many remedies tried during that time. The quick and complete relief which the drug afforded in my case was, therefore, quite astounding to Dr. Speidel and myself. Throughout the remainder of that season—I was able to keep myself absolutely free from symptoms by the ingestion of this acid, and have continued its use each year since that time with the same satisfactory results. During the eight years since this initial experience with the drug—I have used it in 16 other cases, making with my own a total of 17 cases. As I am not engaged in active practice these have been in no sense picked cases, but only such as have come to my attention in the persons of acquaintances and coworkers. All of these individuals present undoubted cases of hay fever, all have been rendered practically symptomless by the drug, and all have been able to obtain this relief each year in which they have used the drug.* The patients were of both sexes and ranged in age from eight to seventy-two years. Three individuals had taken the pollen-desensitization treatment; two of these had obtained little or no relief, the third had suffered such violent local and constitutional reactions that the treatments were stopped before completion of the series. One patient had been greatly relieved during one season by the daily

* There was one other case which can be disposed of as follows: Prescribed for through a third person (layman); the drug (which probably deteriorates rapidly) was carried about for several months during the patients travels abroad and only taken upon his return to this country toward the close of the hay-fever season; reported, through the third person, that he "didn't think it helped him much." No evidence that the drug was taken at proper intervals or, indeed, of the actual existence of the malady in this individual.

ingestion of calcium lactate for seven months prior to the hay-fever season. All of them had at various times obtained slight and transient relief from topical applications. Thus, it would seem that these are 17 typical cases of the malady. All of them have obtained practically complete freedom from symptoms by beginning the ingestion of the acid at once on the appearance of the first premonitory symptoms and continuing its use four times daily throughout the duration of their particular "season." The importance of the midnight dose, as well as the rapidity with which the sufferer comes under or escapes from the influence of the drug, is shown in the following report.

Case Report.—M. J., white man, aged forty-two years. Office worker, dates the beginning of his attacks very definitely from visit to farm at age of sixteen years. Since that time he has lived in large cities in Tennessee, New York, Illinois and Wisconsin, and has had an annual attack of the malady, beginning usually about the middle of August and lasting approximately to the middle of September. Skin tests: goldenrod, positive; ragweeds, strongly positive; goldenglow, positive.

August 18. Symptoms fully established for four days. Nitrohydrochloric acid (U. S. P. full strength) prescribed, 10 drops in a glass of water to be taken after each meal and upon retiring (as near midnight as possible). First dose taken at noon.

August 19. Symptoms very little abated in the forenoon but markedly decreased in the afternoon (had always been as violently afflicted in P.M. as in A.M.).

August 20. No symptoms.

August 21. No symptoms.

August 22. No symptoms.

August 23. No symptoms (midnight dose omitted).

August 24. Slight "itching behind the eyes" on rising in the morning. Morning and noon dose omitted. Violent symptoms began at noon and persisted throughout remainder of the day. Evening and midnight doses taken.

August 25. Drug continued. No symptoms.

August 26 to September 20. Drug continued. No symptoms.

September 21. Drug discontinued. No symptoms thereafter; season over.

Routine of Administration. In the first few cases I prescribed the acid to be dropped (10 drops) into water just before taking, but soon found this method open to the following objections: (1) Very few druggists have on hand Acidum Nitrohydrochloricum which fulfills the requirements of the U. S. P. IX; (2) such as are willing to prepare a fresh product are reluctant to dispense it, looking upon 10 drops of "aqua regia" (the "official" dose is 3 minims) as dangerous; (3) the full-strength acid is so corrosive that its handling in the household is very difficult. Latterly I have, therefore, written the following prescription:

℞—Acid. nitrohydrochl. (*not* the dilute) . . . . . ℥ivss (18.0)
Aq. dest. q. s. ad . . . . . ℥iv (120.0)
M. et ft. sol.
Sig.—1 teaspoonful in ¾ glass of water, followed by another glass of water, after each meal and again upon retiring (as near midnight as possible).

This prescription has the advantages for routine prescribing that it is free from the fuming noticeable to the patient as he counts the drops of the stronger preparation, and that it can be dispensed in the usual bottle with the ordinary cork stopper. It will be noted that the prescription will not provide 10 minims to each teaspoonful dose if we accept the dram and teaspoonful as equivalents, as is usually done. Writing the prescription on this usual basis of 8 drams, and therefore eight teaspoonfuls to the ounce, the patient will really get more than 10 minims in each dose, since there are actually only between six and seven average teaspoonfuls in an ounce. This added acidity is enough to make the taste of the preparation objectionable to some people. Therefore, I have computed the proportions on the basis of the actual teaspoonfuls, and not drams, to the ounce. The result is a pleasantly acid but not corrosive tasting mixture. The ingestion of the acid, even in this large dose, cannot be looked upon as in any sense dangerous. One precaution, however, I have always taken, namely, that of forbidding the use of any laxatives or purgatives not prescribed by me, as there is perhaps some danger of calomel being converted by the acid into corrosive sublimate.

Historical. In 1893, Bishop[3] proposed the uric-acid theory of hay fever in the first prize essay of the United States Hay Fever Association and advocated the theory at the meeting of the American Medical Association the same year. Learning in 1894 that Tyrrel, of Toronto, had published a paper in 1892[4] advocating the same theory, he readily accorded full credit to Tyrrel for his work. The use of nitrohydrochloric acid upon purely theoretical grounds was advocated by Bishop. However, the excellent results obtained by him were soon lost sight of in the welter of papers then appearing upon the subject of "uric-acid diathesis," to which Bishop himself considerably contributed. Also the causal relationship of pollens to the disease was beginning to be urged at this time, and further contributed to push the newly advocated drug into the background before it had had any sort of fair trial. Certainly, I can find no account of its extensive use with a report of the findings anywhere in the literature between 1897 and this present time. However, that it was being used, and with excellent results, by private practitioners here and there over the country is evidenced by the reports of these practitioners which occur now and then during this period. I shall cite only one of these reports as evidence of the degree of success with which the casual users of the drug were meeting. In the *Journal of the American Medical Association*, January 31, 1903 (**40**, 332), a paper of Lockard[5] is abstracted as follows, after describing other local and general measures employed: "In all cases he administers nitromuriatic acid (not the dilute), 3 to 5 drops after meals and before retiring. The acid is almost a specific; in the great majority relief is almost immediate."

A number of prominent otolaryngologists in various parts of the country have told me that they have never heard of the drug, though Gleason[6] mentions it in the 1924 edition of his text in almost precisely the same words used in the 1914 edition, and in how many editions before that I do not know.

I submit that we have overlooked a drug which may be of the utmost value in the treatment of hay fever.

Present Status of the Desensitization Treatment. As one of the reasons for my advocacy of nitrohydrochloric acid at this time, I have mentioned the considerable failure of the pollen desensitization methods. That they have failed to a considerable degree is evident, I believe, in the reports published by workers in this field. Arranging several of these reports as in the accompanying table, it will be seen that the number of cases completely relieved ranges from 9 per cent to 29.6 per cent, and that the number obtaining no relief is practically the same, 9.1 per cent to 28 per cent, with the other cases falling somewhere in between. Piness[9] states that the average

		Relief afforded by preseasonal immunization.			
Authority.	No. cases.	Complete relief, per cent.	Marked relief, per cent.	Slight relief, per cent.	No relief, per cent.
Vander Veer[7] . . .	1744	23.0	49.0	18.0	10.0
Rackeman[8] . . .	91	9.0	62.0	....	28.0
Piness[9]	202	29.6	40.0	21.4	9.1

of complete relief obtained by all workers is about 23 per cent. Also it is to be borne in mind that some of those who obtain no relief are actually made worse by the treatment; one writer, Caulfeild,[10] places this number at 2.3 per cent of the total number treated. Furthermore, both local and constitutional reactions are of frequent occurrence and both types are oftentimes severe. For instance, Piness[9] reports that in 202 cases, local reactions occurred in 132 patients and that constitutional reactions occurred 17 times. This writer further states "the greatest percentage of reactions occurring in those patients who received the greatest measure of relief, which is in accord with the experience of others."

In view of the above, a fair statement of the present status of preseasonable desensitization with pollen substances would seem to be as follows: Hay-fever sufferers, who will submit to the subcutaneous injection of the pollen antigens once each week for four to six months prior to the beginning of their symptoms, have a 9 to 29 per cent chance of having those symptoms averted; also they have a 9 to 28 per cent chance that the symptoms will not be relieved at all; also they have a 2 to 3 per cent chance that the symptoms will be worse than they have ever been before; also a considerable number of the patients, especially among those who are relieved, will have to undergo local and constitutional reactions of varying severity.

These statistics are not very impressive. Indeed, it would seem to me that it is time for the workers in our established hay-fever clinics to begin the examination of other possible remedies while they are continuing their pollen investigations.

Suggestions for Study. Granting that nitrohydrochloric acid is deemed worthy of a trial in one or more of the large hay-fever clinics in this country, I would suggest that the work be planned to cover the following points:

1. Clinical effects of the acid when taken at once after dilution (the drop method employed in my early cases).
2. Clinical effects of the acid when taken in some such form as the prescription embodied in this paper.
3. Effects of age upon the efficacy of the acid, either full strength or diluted.
4. Full studies of the blood chemistry of hay-fever sufferers and the alterations induced in same by the acid.
5. Other studies planned to elucidate the rationale of the method.

The pharmacologic problems which suggest themselves in connection with this work are of tempting interest, but since they are all capable of being investigated upon actual hay-fever sufferers, it is my belief that at least the initial studies should be made in the clinic.

Summary. The author's quite astounding results from the employment of nitrohydrochloric acid in the treatment of 17 cases of hay fever, in conjunction with similar reports of private practitioners scattered through the literature of the past thirty years, lead one to believe that perhaps we have heretofore neglected an important remedial agent. It is suggested in the paper that studies of the effects of this drug be made in one or more of the established hay-fever clinics, and that such studies would be timely since the pollen desensitization work has met with only qualified success up to the present time.

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PRIMARY INVOLVEMENT OF THE UPPER EXTREMITIES IN THROMBOANGIITIS OBLITERANS (BUERGER'S DISEASE).

By George R. Constam, M.D.,
FELLOW IN MEDICINE, THE MAYO FOUNDATION, ROCHESTER, MINN.

More than 80 per cent of all cases of thromboangiitis obliterans seen at the Mayo Clinic have been incorrectly diagnosed previously. Presenile gangrene, juvenile gangrene, endarteritis, endophlebitis, endangiitis obliterans, primary endarteritis obliterans, and spontaneous gangrene are terms applied to the affection by different authors. Buerger seems to have been the first to review, clinically and pathologically, a large group of these cases. He named the disease thromboangiitis obliterans, a term which, if generally accepted, would greatly facilitate mutual understanding of the subject.

Brown classifies vascular lesions in two main groups, functional and organic. In the first group there may be vasomotor disturbances of a vasoconstrictor or vasodilator nature caused by vascular spasm or paralysis. In the second group the circulatory insufficiency is due to organic blocking of a bloodvessel. Thromboangiitis obliterans, arteriosclerotic endarteritis obliterans, traumatic thrombosis, and so forth, belong to the second group. In the first group Raynaud's disease demonstrates a vasoconstrictor disorder; erythromelalgia, vasodilator disorder. In Raynaud's disease pulsation in a main vessel is said by certain investigators to be absent during the stage of syncope only.* It is never found in primary erythromelalgia and in the other types of vasomotor neurosis.

The characteristic lesion in thromboangiitis obliterans is an inflammatory thrombosis involving not only the larger veins and arteries, but also their finest branches, even the capillaries. Fig. 1 shows a typically affected branch of an anterior tibial artery. There is organized thrombus of the vessel, cellular infiltration of all the layers of the vessel wall, and fibrosis of the perivascular tissue. The attention of those who are interested in the anatomic aspects of the disease is directed to the work of Winiwarter, Borchard, Dutil and Lamy, Buerger, Smith and Wells, Patterson, and others.

The cause of the disease is unknown. Certain clinical and histologic criteria point to an infectious origin. Trauma, mechanical, thermal or chemical (tobacco), probably plays a precipitating part.

In most cases the first symptoms appear in the lower extremities. The hands and arms become affected later, if at all. In only 24 of a series of 94 cases observed at the Mayo Clinic were symptoms due to lesions of the upper extremities. In four the lesion in the hands was the outstanding clinical observation and apparently

* This has so far never been observed at the Mayo Clinic.

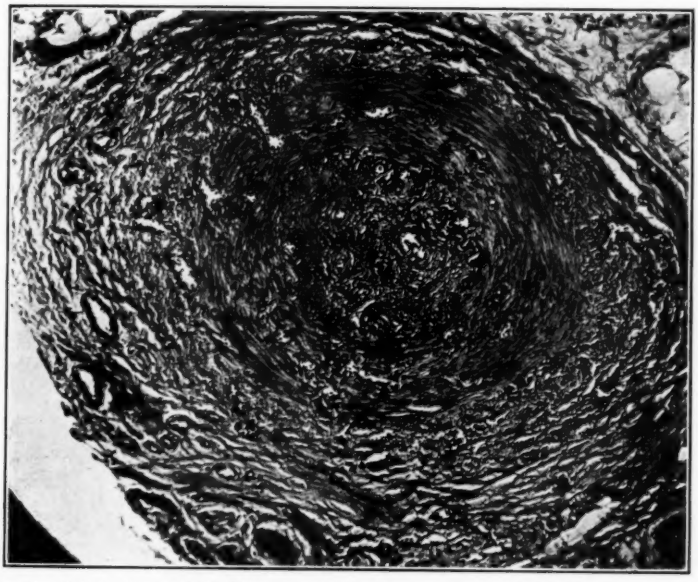

FIG. 1.—Thromboangiitis obliterans. Branch of anterior tibial artery. (× 60.)

FIG. 2.—Thromboangiitis obliterans of the hands. Trophic disturbance at tip of second finger.

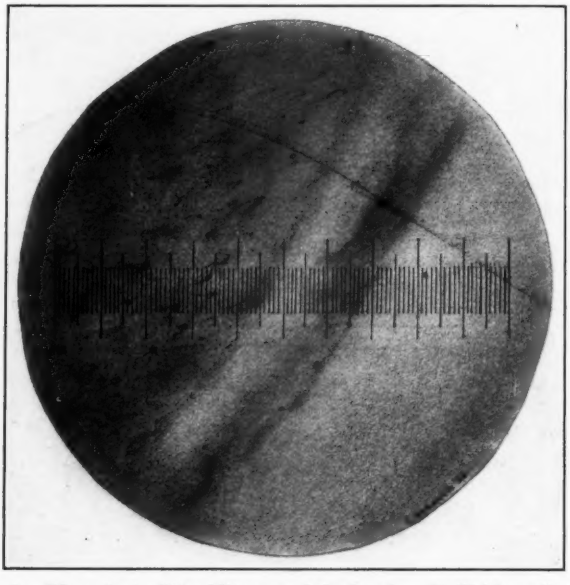

FIG. 3.—Thromboangiitis obliterans of the hands. Nailfold capillaries.

FIG. 4.—Subcutaneous fibrous tissue from finger in thromboangiitis obliterans. (× 60.)

FIG. 5.—Small vessels and capillaries in the subcutaneous fibrous tissue of a finger in thromboangiitis obliterans. (× 120.)

they were involved primarily. These 4 cases are reported because thromboangiitis obliterans of the hands is frequently incorrectly diagnosed.

Report of Cases. CASE I.—An aviator, of Scotch-Irish descent, aged forty-three years, had been well until December, 1923, when during an aëroplane flight he received a severe mental shock by witnessing a fatal accident to a friend, and was exposed to a change in temperature from 100° to 0° F. within forty minutes (altitude 16,000 feet). During this flight, which lasted three and a half hours, his right hand was constricted by an unusually tight glove, the fourth finger especially suffering from lack of circulation. When taking off this glove he noticed that the distal phalanx of his fourth finger was white, numb, and cold. There was some pain in the third, fourth, and fifth fingers, in the wrist and on the inner side of the right arm, up to the axilla. The skin of the fourth finger soon became leathery and about ten days later four small, dark colored, very tender gangrenous areas appeared at its tip. Three of these areas sloughed, ulcerated and healed at various times during the spring of 1924. These signs were interpreted as being due to acute arterial insufficiency in the fourth right finger immediately after the flight. The disease remained well compensated until fall, when, aggravated by an automobile trip, the gangrene of the fourth finger became more extensive and the pain intolerable, until finally amputation was necessary. Pain, pallor, and numbness involved the rest of the fingers of the right hand in the following order: October, 1924, the fifth finger, November, 1924, the third finger; September, 1925, the second finger; December, 1925, the first finger. A small area of gangrene had appeared in the tip of the fifth finger in September, 1924, but healed in a few months. Arterial insufficiency in the right leg in the form of intermittent cramps of the calf after exercise, appeared in December, 1924, after the patient had completed a transcontinental flight. A constant wind had forced him to use the right rudder almost continuously, which meant considerable strain on the right leg. A slight injury in January, 1925, started an ulcer on the tip of his right second finger. Repeated mechanical insults in June and July of the same year prevented restitution. In April, 1926, after strenuous manual work the patient noticed that the distal part of his right radial artery had lost its pulsation for the length of about 2.5 cm. A few weeks later, after another strain on his hands, this pulseless segment increased an equal distance proximally.

Examinations at the Mayo Clinic (July 13, and August 2, 1926) revealed hypertrophic rhinitis, a large plica in the tonsillar fossa, and periapical infection of two teeth; there were no changes in the eyes, throat, thyroid, lungs, heart or abdominal organs. Blood, urine and coagulation and bleeding time were normal. Roentgenograms of different parts of the body showed nothing abnormal except old fractures, and calcified vessels were not demonstrated. The distal part of the fourth finger (Fig. 2) had been amputated, leaving a healthy scar. The second finger was slightly swollen, especially at the tip, and bluish-red. The skin was atrophic and glossy, the finger nail brittle and thickened at its lateral borders which were growing into the underlying tissue. A circular ulcer, about 4 mm. in diameter and 3 mm. in depth, was found at the tip of the finger. On elevation of the hand there was distinct pallor of all the fingers from their tips to the middle portions of the proximal phalanges, except in the little finger in which the pallor was less conspicuous. The distal parts were involved to the middle phalanx. In the dependent position marked rubor of all the fingers occurred, especially at the tips, and gradually decreased toward the middle of the hand. There was occasional muscular fibrillation in the ulnar region. The right hand was cooler than the left. The tip of the second finger was tender

to pressure and painful when the hand was dependent. On palpation the radial artery was found to be thickened, cordlike, and pulseless, distally from a point 5.3 cm. from the distal crease of the wrist. Proximally the pulse was palpable but diminished in volume. Only a faint intermittent pulsation was perceptible in the ulnar artery. Pathologic change was not apparent in the left upper extremity. Rubor was exaggerated in the distal parts of both feet in the dependent position. The pulse in the right posterior tibial artery was only intermittently palpable and much impaired in volume. Examination of the nailfold capillaries in the diseased fingers with the capillary microscope disclosed the normal number of capillaries, but they were poorly filled. The loops were short, fine, hazy, and at certain points appeared hooklike (Fig. 3). Flow was not interrupted and capillaries were not enlarged.

A few specimens of the skin of the finger which had been amputated in 1924 were obtained for histologic examination. In a part of the section remote from the areas of gangrene changes were noticeable, which, in the light of recent studies seemed to be characteristic of thromboangiitis obliterans. The perivascular fibrosis around the small vessels of the subcutaneous tissue is conspicuous (Fig. 4). The arterial walls are rich in cells and the endothelium of all vessels, including the capillaries is swollen so much at certain points as to seem to obstruct the vessel (Fig. 4). Fig. 5 shows slight infiltration of the perivascular tissue with polymorphonuclear and round cells. This is probably a superimposed secondary process due to the proximity of the gangrenous area. In view of these observations and the history of slowly progressive arterial insufficiency the diagnosis of thromboangiitis obliterans was made.

Case II.—An electrician, a gentile, aged thirty years, was admitted to the Mayo Clinic in July, 1924. His work exposed him frequently to electrical shocks. He smoked about twenty cigarettes a day. For several years he had had difficulty in keeping the tips of his fingers and toes warm during cold weather. Cramps had been present intermittently in both feet for one and a half years. His fingers became first red and then blue when exposed to cold. In August, 1922, he cut the right second finger. Healing was slow. Shortly after this gangrene developed spontaneously in the right third finger and later in the first finger of the right hand and in two fingers of the left. Finally the right first toe became gangrenous.

With the exception of the extremities the general physical, Roentgen ray, and laboratory examinations including the Wassermann test of the blood were negative. The upper extremities were cold to the wrist, the nails ridged and cyanotic. There were dry ulcers on the tips of the second and third fingers on both hands. The radial pulse was palpable on both sides, but the arterial wall seemed to be thickened. The left lower extremity was normal. The right first toe was partially sloughed off. There was a small fissure at the base of the right fifth toe. In the dependent position there was marked rubor and cyanosis of both feet. On elevation there was pallor of both feet and ankles. When the legs were suddenly lowered to the dependent position a marked delay in the return of color was noted. Pulsation could not be felt in the right dorsalis pedis artery. In the right posterior tibial and popliteal arteries it was diminished in volume. On the left side vessels were not palpable below the femoral artery. The diagnosis was thromboangiitis obliterans. Contrast baths, baking, and postural exercises (Buerger) were advised.

In February, 1926, the patient wrote, "A strong pulse can be felt in the back of my wrist, but none in the usual places, and another one can be felt on the top of my instep." He was walking regularly and even played nine holes of golf.

CASE III.—An engineer, gentile, aged thirty years, was examined in the Mayo Clinic in November, 1925. He had smoked an average of twenty cigarettes daily for the last seven years. In January his left index finger was crushed, but it healed normally in two weeks' time. Six months later the first symptoms of his complaint appeared in the form of "rheumatic pain" in the fingers and hands. In August small dry ulcers appeared spontaneously on the tips of the right second and third fingers. If the fingers were exposed to cold they became cyanosed and painful, but if warm they were red and free from pain. A few weeks later the entire right hand had become involved, and the left hand chilled easily. In October he had pain in the arches of both feet after exercise (foot claudication).

The results of physical and laboratory examinations were negative except for the extremities. There was marked cyanosis of the distal parts of the right second and third fingers. Small dry ulcers had developed at the tips of the affected fingers with thickening of the surrounding skin. In the dependent position there was intense rubor, and with elevation patchy pallor of the entire hand. The radial and ulnar arteries were open, but their pulsation was diminished. In the dependent position the left hand showed faint rubor, and the radial pulse was diminished in volume. No other sign of circulatory disturbance was detected. There was marked rubor of the toes of both feet in the dependent position and intense pallor in the elevated. Pulsation was scarcely perceptible in either dorsalis pedis artery. The other vessels seemed to be normal.

A diagnosis was made of thromboangiitis obliterans of all the extremities. Without a careful history in this case Raynaud's disease might have been suspected. None of the palpable vessels was completely obstructed. Diminished pulsation of a peripheral vessel, if observed by an experienced clinician, is a fairly reliable sign. The marked change in color with change in position and the impaired pulsation without other signs of disease excluded Raynaud's disease.

A few injections of a foreign protein (triple typhoid vaccine), contrast baths, baking, and postural exercises caused the ulcers to heal rapidly. Reëxamination of the patient, ten months after his first examination, showed remarkable improvement of the circulation in the upper extremities, but no change in the legs. The ulcers of the finger tips had disappeared completely. Except for faint rubor if the hands were dependent for five minutes or longer and the fact that they easily become cold, there were no signs of disturbance in the blood supply.

CASE IV.—An engineer, of Scotch-Irish descent, aged forty-six years, was examined at the Mayo Clinic in February, 1926. In August, 1925, he had pinched the fourth finger of his right hand. The skin was not broken but the finger turned black and seemed to shrink and dry up. Gangrene developed, extending slowly up to the base of the finger. The hand became swollen and the finger extremely tender and painful. In December disarticulation was performed at the distal interphalangeal joint. The stump did not heal and one week later an ulcer appeared on the first finger of the other hand. During the winter of 1923 and 1924 there were signs of impaired circulation in the left foot, that is, numbness of the sole and pallor of the toes when exposed to cold. These symptoms disappeared with the warm season. Exactly the same features appeared during the next two winters (1924 and 1925, and 1925 and 1926) in the opposite extremity, while the left foot remained without symptoms.

Except for the extremities, the results of physical and laboratory examinations were negative. Roentgen ray examination did not reveal any calcified vessels. The wound from amputating the right fourth finger did

not heal and a small ulcer still remained at the tip of the left first finger. All fingers of both hands showed mild rubor in their distal parts when dependent and pallor when elevated. Pulsation could not be felt in the right ulnar and left radial artery. The left ulnar pulse was weakly intermittent; the right radial and the brachial arteries pulsated normally. In the dependent position there was considerable rubor of all the toes, but more especially in the right foot. On elevation there was marked pallor of the feet and residual rubor in the first toe. Pulsation could not be detected in the right posterior tibial and the left dorsalis pedis arteries. The other vessels were open.

A diagnosis was made of thromboangiitis obliterans. Under the usual measures, such as postural exercises and contrast baths, both areas of gangrene healed in four weeks, but one week later an ulcer formed at the tip of the right second toe and soon afterward one on the right first toe. They were associated with such severe pain that the patient reëntered the hospital during the first part of June, three months after his first dismissal. Except for the right foot and hand the condition was the same as when the patient was first examined. The pulse of the right dorsalis pedis artery was only intermittently palpable and the anterior part of the foot was swollen. The distal part of the second toe was covered by black mummified skin, and there was a small superficial ulcer lateral to the nail of the first toe. The wounds of the right hand were healed.

Bilateral lumbar sympathetic ganglionectomy (second, third, and fourth lumbar ganglions) was performed (Adson). The patient left the hospital twenty days after the operation, completely relieved from pain. The skin temperature of his feet had increased about 6° C. Pulsation was constant in all the vessels of both feet. The ulceration of the right first toe seemed to be healing, while in the right second toe there was a progressive line of demarcation. It is too soon to report on the efficacy of this operation.

Discussion. In every case of peripheral vascular disease a complete general examination is indispensable and the main vessels of all extremities should be palpated repeatedly. Three groups of objective symptoms must be looked for: (1) Pulseless vessels; (2) signs of vascular insufficiency; (3) vasomotor phenomena. Constant absence of pulsation in one or more of the main vessels without signs of vascular insufficiency or a history of a progressive involvement is suggestive of a well compensated organic lesion, but alone is not sufficient evidence for a definite diagnosis. Congenital abnormalities in position or development of vessels can imitate a lack of pulsation in the typical places. Erb found in 4 of 381 cases absence of pulsation at one or two points in the feet without coexistence of demonstrable peripheral vascular affection. It is doubtful whether the pulsation of a larger vessel disappears during an attack of Raynaud's disease. If this does take place the vessel is said to open as soon as the paroxysm of vasoconstriction ceases.

Signs of vascular insufficiency, that is, exaggerated rubor in the dependent position, pallor on elevation, exaggerated or retarded reactionary rubor, and rubor occurring from changing from the elevated to the dependent position are, if constant, characteristic of an organic affection. Vasomotor phenomena (rubor, pallor, cyanosis, and so forth) occur in both organic and functional diseases.

Only if no signs of an organic affection can be found is it justifiable to diagnose primary functional vascular disease.

Organic vascular affections often start with vasomotor disturbances and these alone may be present in early stages. Intermittent pallor and cyanosis are initial symptoms of thromboangiitis obliterans of the hands and are frequently mistaken for symptoms of Raynaud's disease. As Allen and Brown pointed out recently, heat never leads to such a complete compensation or overcompensation of these vasomotor symptoms in the former affection as it does in the latter. Thromboangiitis obliterans should always be suspected, even in the presence of pulsating vessels, in case of a vascular affection in the male sex.

The absence of demonstrable calcified arteries, the age of the patient, and the marked rubor of the fingers and toes made a diagnosis of endarteritis obliterans on an arteriosclerotic basis untenable. In the upper extremities, arterial insufficiency from thromboangiitis obliterans is more common than arteriosclerotic endarteritis.

The history and all data of these cases were negative in regard to a former or present syphilitic infection. The clinical development and the anamnesis enabled us to eliminate embolism, traumatic thrombosis, postinfectious arteritis, influenza, pneumonia, and so forth, and carbon monoxid poisoning.

The compression of the right hand by a tight glove in Case I and the pinching of the fourth finger in Case IV were probably the inciting causes for the outbreak of the disease which might have been present in a latent stage. Borchard described the condition in the upper extremities of a fisherman and attributed it to the frequent exposure of his hands to cold water. The histories in Cases II and III do not account for the appearance of the affection.

Thromboangiitis obliterans of the upper extremities rarely leads to gangrene of more than a few fingers. In nearly all cases the lower limbs also are sooner or later affected. The process localized in the lower extremities is usually much more mutilating. Therefore, in all cases of thromboangiitis obliterans of the hands, protective measures to the lower extremities are indicated, even if clinical evidence of their involvement is lacking.

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THE RELATIVE VALUE OF CHOLECYSTOGRAPHY AND THE ORIGINAL LYON TEST[1] IN ESTIMATING BILIARY TRACT FUNCTION.[2]

By W. W. Boardman, M.D.,

Associate Clinical Professor of Medicine, Stanford Medical School, San Francisco, Calif.

We have recently had two methods developed for the study of some of the functional activities of the biliary system. This system includes not only the gall bladder, but the liver, the common and cystic ducts, the sphincter of Oddi,[3] and their associated lymphatics. The prime function of this system is the secretion of bile and its discharge into the duodenum. Normally the secretion of bile is a continuous process, but its discharge into the duodenum occurs only during digestive periods. In the interdigestive periods the sphincter of Oddi is tonically contracted, and the freshly secreted bile finds its way into the gall bladder, where it is concentrated and stored. As a result of this concentration, the gall bladder bile is darker in color and more viscid in consistency than the liver bile. With the relaxation of the sphincter of Oddi by normal or artificial stimuli, there is an outflow of this darker and more concentrated gall bladder bile into the common duct and eventually into the duodenum.

It is evident that for a normal functioning of the biliary system we must have a fairly normal liver, patent common and cystic ducts, a sphincter of Oddi capable of closing the outlet of the

[1] For the purposes of this paper I have taken the liberty of designating the intraduodenal administration of magnesium sulphate solution and the observation of the resulting bileflow as the "Original Lyon Test."

[2] Read before the American Gastroenterological Association, Atlantic City, May, 1926.

[3] Whether the closure of the lower end of the common duct is dependent upon the tonic contraction of the sphincter of Oddi or to the tonus of the duodenal wall is still to be decided.

common duct, and a gall bladder whose walls are sufficiently elastic to expand and contract, whose epithelial lining and lymphatic system are intact, allowing of concentration, and whose lumen is not filled by gall stones, polypi, inspissated bile, or new growths. It is equally evident that a disturbance in any one or more of these conditions will result in an abnormal functioning.

The original Lyon test attempted to determine the functional activity of the system by a study of the bileflow following the artificial relaxation of the sphincter of Oddi, by a solution of magnesium sulphate. Accepting for the present that "B" bile is the concentrated gall bladder bile, more or less diluted with common duct bile, it is evident that the recovery of "B" bile is indicative of patent common and cystic ducts, a gall bladder capable of concentrating and discharging its contents, and probably a fairly normally acting sphincter of Oddi. On the other hand, failure to recover "B" bile in an otherwise satisfactory test would suggest an obstruction of the cystic duct, disturbed gall bladder function, or an open sphincter of Oddi.

Cholecystography, as proposed by Graham, attempts to determine the functional activity of the system by the radiographic study of the gall bladder region after the oral or intravenous administration of one of the heavier halogenated phenolphthaleins. Normally these dyes are excreted in the bile, carried to the gall bladder, and there concentrated to a sufficient degree to offer marked resistance to the Roentgen ray, with the resulting production of beautifully distinct shadows of the dye-filled gall bladder. By this means we are enabled to study the size, shape and position, but more especially the filling, the concentrating function and the emptying of the gall bladder. Successful visualization is dependent upon a sufficient concentration of the dye in the blood and a normally functioning biliary system. Partial or complete failure of visualization in an otherwise satisfactory test suggests obstruction of the cystic duct, disturbance in gall bladder function, or an open sphincter of Oddi.

It is thus evident that these two new methods of studying biliary tract function are dependent upon the same functional activities, and on theoretical grounds at least, conditions leading to an abnormal response in the one test might be expected to do the same in the other. To test this conclusion we have used both cholecystography and the original Lyon test in a series of cases taken from the gastrointestinal service of the Stanford Medical School.

In the Lyon test we have followed the usual procedure, confirming the location of the tube by fluoroscopic examination. The time of appearance, the character and amount of the "B" bile has been noted, but no systematic study of the microscopic, chemical or bacteriologic features has been attempted in this series.

For cholecystography we have used both the oral and intravenous

methods of administration. For the oral method we have followed the plan proposed by Whitaker. For the intravenous method, we at first administered the dye at 8 A.M., but later adopted the plan proposed by Sossman of giving the dye at 10 P.M. In the majority of the later cases, following the fourteen-hour examination, the duodenal tube was introduced, and the usual Lyon test performed, following which a third examination was made. In some of these cases, cream or olive oil was then administered through the tube or orally, and a fourth film taken an hour later. By this means we have been able to compare directly the evidence of emptying of the gall bladder after magnesium sulphate as furnished by the Lyon test with the evidence furnished by cholecystography, and also to compare the degree of emptying after magnesium sulphate with that occurring after cream, olive oil, or a fatty meal.

In analyzing the results of the Lyon test, we find that they fall into three distinct groups, depending upon the color of the "B" bile. In the first of these the "B" bile is very dark brown, in the second group it is a deep golden brown, and in the third there is no "B" bile.

Similarly, the results after cholecystography fall into three groups: The first showing normal visualization as defined by Graham, the second showing incomplete visualization, and the third showing no visualization.

It is generally recognized that a total or partial failure of visualization, after the oral administration of the dye does not necessarily indicate a functional disturbance of the biliary system, but may depend upon faulty intestinal absorption. In 25 of our cases in which the dye was administered, both orally and intravenously, there was agreement in 9, or 36 per cent, and disagreement in 16, or 64 per cent. In every case of disagreement the intravenous method gave evidence of a more normally functioning biliary system, as shown in Table I. These findings emphasize the fact that after oral administration only the evidence of a perfectly normally functioning tract is to be accepted. In this series, therefore, only cases showing normal visualization after oral administration have been included.

TABLE I.—THE LACK OF AGREEMENT IN THE CHOLECYSTOGRAPHIC FINDINGS IN TWENTY-FIVE CASES AFTER ORAL AND INTRAVENOUS ADMINISTRATION OF TETRAIODOPHENOLPHTHALEIN.

	Results.		
Method.	Normal.	Incomplete.	No visualization.
Oral	0	12	13
Intravenous	12	10	3

Agreement in 9 or 36 per cent.
Disagreement in 16 or 64 per cent.

Again, no case has been included that did not give a good flow of "A" bile following the introduction of the salts. In many of the cases repeated tests have been performed, and in the majority the "B" bile has been of constant character.

We have for comparison a total of 61 cases. Five had the dye by mouth only; 25 had the dye both orally and intravenously, and 31 had the dye only intravenously.

TABLE II.—THE TYPE OF "B" BILE OBTAINED IN SIXTY-ONE CASES AFTER ADMINISTRATION OF MAGNESIUM SULPHATE SOLUTION COMPARE WITH THE RESULTS AFTER CHOLECYSTOGRAPHY.

Cholecystography.		Lyon—"B" bile.		
Result.	No. of cases.	Dark brown. Per cent.	Golden brown. Per cent.	Absent. Per cent.
Normal	37	**54**	35	11
Incomplete	18	28	**44**	28
No visualization	6	17	33	**50**

An examination of Table II, in which are recorded the results after cholecystography and Lyon drainage, shows the dark brown "B" bile most frequently present with normal visualizations, the golden brown "B" bile with incomplete visualizations, and the absence of "B" bile with failure of visualization. However, this agreement is only 50 per cent complete, and the question arises as to which test furnishes the more reliable information regarding the functional activity of the biliary system.

TABLE III.—THE DEGREE OF EMPTYING OF THE GALL BLADDER AND THE TYPE OF "B" BILE OBTAINED AFTER THE INTRADUODENAL ADMINISTRATION OF MAGNESIUM SULPHATE SOLUTION IN ELEVEN CASES COMPARE WITH NORMAL CHOLECYSTOGRAPHIC FINDINGS.

Result after cholecystography.	Result after Lyon test.	No. of cases.	Degree of emptying shown radiographically after Lyon drainage.		
			Marked.	Slight.	No
Normal	Dark brown "B" bile	5	5		
Normal	Golden brown "B" bile	4	..	3	1
Normal	No "B" bile	2	..	..	2

In Table III we have arranged the results in 11 cases in which the Lyon drainage was performed fourteen hours after the intravenous injection of the dye. By this means we have been able to compare the character of the "B" bile obtained after Lyon drainage with the degree of emptying of the dye-filled gall bladder, as shown radiographically after the same drainage. The table shows quite clearly that the dark brown "B" bile was obtained in those cases

showing marked decrease in the size of the gall bladder, the golden brown "B" bile in those showing slight or no appreciable decrease in size, and the absence of "B" bile in those showing no decrease in size. From this it is suggested that the character of the "B" bile is dependent upon the degree of emptying of the gall bladder. If this be true, it is important to determine whether or not magnesium sulphate, as used in the Lyon test, is the most efficient stimulus for the emptying of the gall bladder.

TABLE IV.—THE DEGREE OF EMPTYING OF THE GALL BLADDER OBTAINED AFTER THE ADMINISTRATION OF CREAM, OLIVE OIL OR A FATTY MEAL COMPARE WITH THE TYPE OF "B" BILE OBTAINED AFTER MAGNESIUM SULPHATE IN TEN CASES WITH NORMAL CHOLECYSTOGRAPHIC FINDINGS.

Result after cholecystograph.	Result after Lyon test.	No. of cases.	Degree of emptying shown radiographically after cream, olive oil, or fatty meal.		
			Marked.	Slight.	No
Normal	Dark brown "B" bile	4	4		
Normal	Golden brown "B" bile	4	4		
Normal	No "B" bile	2	2		

Table IV throws some light on this question. Here we have tabulated the results in 10 cases in which cream, olive oil or a fatty meal was administered following the fourteen-hour examination, and the effect on the dye-filled gall bladder recorded radiographically This result is compared with the character of the "B" bile obtained after Lyon drainage. It will be seen that in 4 cases giving golden brown "B" bile, and 2 cases giving no "B" bile, there was marked decrease in the size of the gall bladder after the administration of cream, olive oil, or a fatty meal.

TABLE V.—RESULTS AFTER CHOLECYSTOGRAPHY AND LYON DRAINAGE, COMPARED WITH THE DEGREE OF EMPTYING OF THE DYE-FILLED GALL BLADDER SHOWN RADIOGRAPHICALLY AFTER LYON DRAINAGE, AND LATER AFTER THE ADMINISTRATION OF CREAM OR OLIVE OIL.

Result after cholecystography.	Result after Lyon test.	No. of cases.	Degree of emptying shown radiographically after Lyon drainage followed by olive oil or cream.					
			Marked.	Slight.	No.	Marked.	Slight.	No.
Normal	Dark brown "B" bile	1	1	..	..	1		
Normal	Golden brown "B" bile	3	..	2	1	3		
Normal	No "B" bile	2	..	..	2	2		

Table V is even more convincing, as here are recorded the findings in 6 cases in which cream or olive oil was administered orally or through the tube at the completion of the Lyon test, and the result recorded radiographically. It will be seen that in 3 cases giving golden brown "B" bile after Lyon drainage and showing slight or no appreciable decrease in the size of the dye-filled gall bladder, there was a marked decrease in size after the administration of fat, and that a similar result was obtained in 2 cases giving no "B" bile and showing no decrease in size after the Lyon. This indicates that magnesium sulphate, as used in the Lyon test, fails to produce an appreciable emptying in some gall bladders capable of free emptying when other stimuli are used.

TABLE VI.—COMPARISON OF FINDINGS BY CHOLECYSTOGRAPHY AND LYON TEST IN ELEVEN OPERATIVELY PROVEN CASES OF CHOLECYSTITIS.

Result after cholecystography.	No. of cases.	Result after Lyon test.		
		Dark brown "B" bile.	Golden brown "B" bile.	No "B" bile.
Normal ?	1	..	..	1
Incomplete	7	4	2	1
No visualization . . .	3	1	..	2

Finally, in Table VI we have tabulated the results obtained by cholecystography and the Lyon test in 11 cases of operatively proven cholecystitis. Here it will be seen that no "B" bile was obtained in 1 case showing practically normal function by cholecystography, whereas dark brown "B" bile was obtained in 4 cases showing no visualization. The findings therefore in this particular group differed widely in the two tests. However, the results by cholecystography very closely paralleled the pathologic findings—stones, marked loss of epithelium, or thickening of the wall being found in every case. From this it seems evident that in some definitely pathologic gall bladders, which by cholecystography show evidence of disturbed function, the Lyon test may cause a sufficient discharge of gall bladder bile to produce a normal appearing "B" bile.

Conclusions. Without attempting to argue any of the numerous questions raised by this subject, such as Sweet's suggestion that the contents of the gall bladder do not pass out by the cystic duct, or the question of the origin of "B" bile, the following conclusions seem justified:

1. Cholecystography, by the oral method of administration, is at present only reliable if normal function is demonstrated. Findings other than normal should be checked by the intravenous method.

2. There is approximately a 50 per cent agreement between the evidence of functional activity of the biliary tract as furnished by cholecystography and by the "B" bile of the Lyon test with magnesium sulphate.

3. The character of the "B" bile obtained after a Lyon drainage is apparently dependent upon the degree of emptying of the gall bladder. Dark brown "B" bile occurring with marked emptying, golden brown "B" bile with slight emptying.

4. The magnesium sulphate as used in the Lyon test may fail to induce emptying in a gall bladder capable of emptying in response to other stimuli.

5. Also the magnesium sulphate may induce sufficient emptying in some definitely pathologic gall bladders to produce a normal "B" bile, although cholecystography shows definite evidence of disturbed function.

From this, it is apparent that the original Lyon test, when used as a measure of biliary-tract function, is less dependable than cholecystography. In fairness to the Lyon test, it must be emphasized that in the hands of careful experienced investigators the examination of the sediment, and in the occasional case the bacteriologic findings, may furnish evidence of pathologic value.

REVIEWS.

OSLER'S MODERN MEDICINE. Volume IV. Reëdited by THOMAS MCCRAE, M.D., Professor of Medicine in the Jefferson Medical College, Philadelphia. Third edition. Pp. 1011, 111 illustrations. Philadelphia: Lea & Febiger, 1927. Price, $9.00.

PART I deals with the Diseases of the Respiratory Tract, including chapters on the Physiology of Respiration, Diseases of the Nasopharynx, Pharynx and Tonsils, Diseases of the Larynx, Diseases of the Bronchi, of the Lungs, of the Pleura, of the Mediastinum, of the Diaphragm; Pneumoconiosis, Pneumothorax. There is also a chapter dealing with the condition of Hypersensitiveness, including hay fever and asthma. Part II is devoted to Diseases of the Circulatory System and includes chapters on General Considerations in Cardiac Disease, Diseases of the Pericardium, The Rate and Mechanism of the Heart Beat, Diseases of the Myocardium, Acute Endocarditis, Hypertrophy of the Heart, Insufficiency and Dilatation of the Heart, Diseases of the Valves of the Heart, Functional Heart Disease, Congenital Heart Disease, Diseases of the Arteries, Aneurysm, Thrombosis, Embolism and Phlebitis, and the Diseases of the Lymphatic Vessels. The work is quite up to the high standard set by the previous volumes of the present and former editions. The reviewer has been particularly interested to note how well the delightful style of the articles originally written by Doctor Osler, notably those on Cardiac Valvular Disease and Aneurysm, has been preserved.

R. K.

PRACTICAL OTOLOGY. By MORRIS LEVINE, M.D. Associate Professor of Otology, New York Post-graduate Medical School and Hospital; Associate Attending Otologist, New York Post-graduate Medical School and Hospital. Pp. 387, 148 illustrations. Philadelphia: Lea & Febiger, 1927. Price, $5.50.

THIS is an excellent book on diseases of the ear prepared especially for undergraduates, general practitioners and postgraduate students. It begins with a clear and full outline of the Anatomy, Physiology, and various diseases to which the ear is subject, and ends with intracranial complications secondary to ear infections. The various operations of the ear, especially the simple and the

radical mastoid operations are so clearly described and illustrated that a beginner will have little difficulty in following. The book is full of excellent therapeutic measures and case histories, and is well worth possessing. D. H.

OBESITY. By LEONARD WILLIAMS, M.D. Pp. 171, 20 illustrations. New York: Oxford Medical Publications, 1926. Price, $3.35.

A BOOK that will prove instructive to the layman and at least amusing to the physician. There is much good sound advice, tinctured with a bit of humor, that makes the book very readable. From the scientific standpoint, however, it must be said that the author is given at times to unwarranted theorizing.

R. K.

SOCIAL FACTORS IN MEDICAL PROGRESS. By BERNHARD J. STERN, PH.D. Pp. 136. New York: Columbia University Press, 1927. Price, $2.25.

PART I gives an interesting discussion of the factors which retard the diffusion of medical discoveries, with an analysis of the specific factors in particular instances: the controversies over dissection, theory of the circulation of the blood, percussion, vaccination, Pasteur's discoveries, antisepsis and asepsis. Part II, on the nature of medical progress, treats of the extent to which an individual contributes to medical advance and the degree of the dependence of such advance upon prior knowledge in medical and other fields. The importance of the latter factors is brought out by an enumeration of many multiple discoveries in the history of medicine.

R. K.

LA ARTERITIS PULMONAR. CARDIACOS NEGROS. By F. C. ARRILLAGA M.D. Pp. 274, 50 illustrations. Buenos Aires: Libreria "El Ateneo," 1925.

A VERY complete account of the history, pathology and clinical picture of a disease in the study of which the author has played a most prominent part. The subject matter is well presented by a master in the field, and anyone with a reading knowledge of Spanish will find this monograph the best source of information on this disease available. The work is profusely illustrated.

R. K.

EXOPHTHALMIC GOITER. By JOHN EASON, M.D., F.R.C.P.E., Physician, Royal Infirmary, Edinburgh. First edition. Pp. 215. Edinburgh: Oliver & Boyd, 1927. Price, 12/6 s.

DESPITE its rather unfortunate title and arbitrary scope, this small volume presents several interesting points of view on various aspects of the problem of hyperthyroidism. A modified conception of the architecture of the thyroid is offered, and another pathologic classification of "exophthalmic" goiter is added to the growing list. The author's clinical observations are, as a rule, shrewd, but his theoretical discussion of relationship between disturbed autonomic function and thyroid disease is confusing. His views as to treatment are not entirely in consonance with those of the majority, and one wonders why some of the cases reported in detail were permitted to continue their courses without operation for so long. The style is not too graceful, and at times becomes irritatingly staccato. In general, however, the book is well worth reading by those particularly interested in thyroid disease. E. R.

NURSING MENTAL AND NERVOUS DISEASES. By ALBERT COULSON BUCKLEY, M.D., Medical Superintendent, Friends Hospital, Philadelphia; Associate Professor of Psychiatry, Graduate School of Medicine, University of Pennsylvania. Pp. 312; 57 illustrations. Philadelphia: J. B. Lippincott Company, 1927. Price, $3.00.

THE importance of this phase of nursing is being recognized more and more, and practical experience in the care of patients suffering with mental and nervous diseases is now regarded as a part of a nurse's basic training. There is a need for good textbooks on this important phase of their work. In the present volume Part I is devoted to a Biologic Introduction; Part II, Mental Processes in Health and Disease; Part III, The Psychoses; Part IV, Diseases of the Nervous Mechanism. The book is well organized, with emphasis, as it should be for nurses, on the outstanding symptoms, nursing care and the need for regarding the patient as an individual. S. G.

LEHRBUCH DER GEBURTSHILFE. By PROF. DR. WILHELM ZANGEMEISTER, Director of the Gynecological Clinic, University of Koenigsberg, Prussia. Pp. 804; 329 illustrations, many partly colored, and 19 colored plates. Leipzig: S. Hirzel, 1927.

A TEXTBOOK on obstetrics for the student and practitioner by a well-known German clinician. The context is well arranged, thor-

oughly complete as to subjects, has an excellent letterpress, is beautifully illustrated, but with a paper binding. The author describes in the preface an ideal system for the training of an obstetrician. Of interest in the descriptive matter of the book are a preference for the immediate emptying of the uterus in eclampsia, a skepticism regarding any advantage in cervical Cesarean section in presumably infected cases, and a healthy conservatism in the handling of puerperal infective conditions. The statistical comments are unusually detailed; the therapeutic suggestions for minor conditions somewhat curtailed.

This would make a splendid book for collateral reading in our American schools. P. W.

OUTLINES OF COMMON SKIN DISEASES. By T. CASPAR GILCHRIST, M.D. Pp. 51; 5 full-page plates of illustrations; indexed. Baltimore: Williams & Wilkins Company, 1927. Price, $1.50.

THIS is a praiseworthy attempt at a species of inexpensive laboratory manual of examination and diagnosis. The brevity of such a presentation is its own apology and explanation for many omissions. The book contains lists of regional distributions; a classification along the old lines; treatment for each individual condition is hinted at; syphilis is considered only from the cutaneous standpoint. Details on which dermatologists will disagree include, for example, the advocacy of Roentgen ray or radium as treatment for lupus vulgaris. Ultraviolet light apparently receives no mention, except as Finsen light. The pictures, while excellent and well reproduced, are reduced to thumbnail size, which obscures some important details. One notices some odd bed fellows, as, for instance, a plate devoted largely to psoriasis with herpes zoster in the lower right-hand corner.

It is to be hoped that other dermatologic teachers will imitate the author in the effort to place before students the actual technique and mechanism of dermatologic diagnosis.

J. S.

THE DE LAMAR LECTURES, 1925–1926. Of the School of Hygiene and Public Health, Johns Hopkins University. Edited, with an Introduction by W. H. HOWELL. Pp. 226, 6 illustrations. Baltimore: Williams & Wilkins Company, 1927. Price, $5.00.

THE De Lamar Lectures in Hygiene were instituted by the Johns Hopkins School of Hygiene and Public Health in 1920 to carry out in part the wish expresses by Joseph R. De Lamar in his will, "to give to the people of the United States generally the benefits of

increased knowledge concerning the prevention of sickness and disease and also concerning the conservation of health by proper food and diet." "The present volume includes only the lectures given in the sixth series, session of 1925–1926, as it has not been feasible to assemble all the material presented in the preceding series, although many of the lectures previously given have found publication in journals of various kinds. The scope of the lectures is very broad. In a few cases they have been historical, but in general they have dealt with the newer ideas and movements that constantly arise in all the many phases of public health work." The lectures are by: David Marine, Alice Hamilton, Francis Carter Wood, Frederick W. Sears, Thomas Adams, W. G. Smillie, Edward R. Baldwin, Louis I. Dublin, Joseph Goldberger, C. R. Stockard, Horace LoGrasso, Robbins B. Stoeckel and Sir Arthur Newsholme.

E. K.

MUSCULAR CONTRACTION AND THE REFLEX CONTROL OF MOVEMENT. By J. F. FULTON, B.Sc. (HARVARD), M.A., PH.D. (OXON.) Pp. 608; illustrations. Baltimore: Williams & Wilkins Company, 1926. Price, $10.00.

IT was a fortunate circumstance that Sherrington was invited to give the Silliman lectures at a time that resulted in the appearance of his monograph in 1906. The first phase of his work was done. The broad features of reflex action had been outlined and the reflex recognized as the functional unit of behavior. The "Integrative Action" epitomizes two decades of work that threw light on a field that had been shadowed with many misconceptions and developed a wealth of data that has stood the test of time. The limitations of the data were due to the limitations of development of methods for recording. The limitations of theory were imposed by the gaps in our knowledge of conduction. Since then two more decades have passed. The foundations for an understanding of conduction, have been laid. The All or None principle has been proved to apply to the axone and to the muscle fiber. Photographic methods, isometric recording of tension, and the string galvanometer have done for the physiology of movement what the microscope did for Anatomy. Clearly it was time for a new monograph.

Those who hoped for a second book from Sherrington's pen have no cause for disappointment that the task has been done by one of the youngest of his pupils. It would be hard to find any one better versed in the subject as a whole, with the clarity of vision that comes from research in many sides of it. The thoroughness with which the work has been done is attested by a bibliography of 1066 references. The historical introduction not only affords a broad perspective of the development of the subject from the forerunners of Galen

to the present day; it vivifies the essential features of each research with quotations so apt that the reader catches the flavor of each personality as though they had been summoned to a physiologic congress at whose discussions he was a privileged auditor.

The book is divided into the two parts indicated by the title. The first half is a discriminating analysis of the data concerning excitation, conduction and contraction, discussing in detail the principles of analysis of electrical and mechanical records. The second half of the book applies these principles to the problems of reflex activity.

In a subject fraught with controversies, the evidence is impartially presented and interpreted. Where a final conclusion is impossible, the alternative explanations are offered and a tentative opinion expressed. With the great majority of these tentative opinions the present reviewer is in accord. In several instances (such as the interpretation of the shortening reaction) the evidence presented has convinced him of the soundness of a view he had not previously held. The book sets a standard in the analysis of data which will do much to improve the quality of future work. On every question dealt with, fresh view points are suggested, questions raised, and the path to their answer is pointed. The book will provoke research.

G. McC.

AMERICAN ILLUSTRATED MEDICAL DICTIONARY. EDITED BY W. A. NEWMAN DORLAND, M.D., Member Committee on Nomenclature and Classification of Diseases of American Medical Association. Fourteenth edition. Pp. 1388, 319 illustrations. Philadelphia: W. B. Saunders Company, 1927. Price: Flexible binding, Plain, $7.00; Thumb Index, $7.50.

FOR twenty-seven years, this has been a standard work. The present, the fourteenth, edition keeps up the high standard set by those that have gone before. Many definitions have been rewritten and over two thousand new words have been added. Illustrations in particular have been added to, to the extent of over one hundred.

R. K.

COMPEND OF PHYSIOLOGY. BY ALBERT P. BRUBAKER, A.M., M.D. Sixteenth edition. Pp. 281; 27 illustrations. Philadelphia: P. Blakiston's Son and Co., 1927.

THE reviewer cannot find in this 16th edition the date of publication of the first edition. Internal evidence points to the later decades of the last century. Many paragraphs of more recent date have converted it into a patchwork of new and old. These revisions leave many important fields untouched. Thus the discussion of

excitation and conduction makes no mention of excitation time, of refractory phase, of decrementless conduction, of the All or None law. It states that the rate of conduction of the nerve impulse is modified by the strength of the stimulus—a conclusion that could have been reached only before the factor of current spread was appreciated. G. M.

DENGUE. ITS HISTORY, EPIDEMIOLOGY, MECHANISM OF TRANSMISSION, ETIOLOGY, CLINICAL MANIFESTATIONS, IMMUNITY, AND PREVENTION. BY J. F. SILER, M.D., MILTON W. HALL, M.D., and A. PARKER HITCHENS, M.D. Pp. 476, 8 illustrations. Manila: Bureau of Printing, 1926.

IN 1922, a Medical Department Research Board for service in the Philippine Islands was created on recommendation of the Surgeon General of the U. S. Army. This Board set itself the task of studying the etiology and mechanism of transmission of dengue, and the present volume represents the fruit of their investigations. While the specific etiology has not been discovered, the authors have been able to show that *Culex* mosquitoes are not vectors of the disease, whereas they have worked out very clearly the details of the mechanism of transmission by *Aëdes*. The work represents a most complete treatise on the disease, including its history, prevalence and distribution, transmission, clinical picture, to the details of which there are a number of original contributions by the authors, immunity studies—also largely by the authors—and the problems of prophylaxis and treatment. There is a very complete bibliography, an appendix with details of the mosquito experiments, case histories, and many technical details in the artificial breeding of mosquitoes. R. K.

MOTHER INDIA. By KATHERINE MAYO. Pp. 440, 41 illustrations. New York: Harcourt, Brace & Co., 1927.

THE book may be summarized in this quotation: "The whole pyramid of the Indian's woes, material and spiritual—poverty, sickness, ignorance, political minority, melancholy, ineffectiveness, not forgetting that subconscious conviction of inferiority which he forever bares and advertises by his gnawing and imaginative alertness for social affronts—rests upon a rock-bottom physical base. This base is, simply, his manner of getting into the world and his sex-life thenceforward." To support her argument the author adduces a wealth of material, much from personal observation and much from authenicated documentary sources bearing on the evils of child marriage, the caste system and the manifold sanitary prob-

lems that arise among a people whose habits are perhaps the most unsanitary in the world today. The author has attacked the problem from the impersonal standpoint of a public-health officer, and although a "layman" has succeeded in making her case remarkably well. Physicians will find the book instructive as well as interesting.

R. K.

TIGER TRAILS IN SOUTHERN ASIA. BY RICHARD L. SUTTON, M.D., Sc.D., LL.D., F.R.S. (EDIN.), Fellow of the Royal Geographical Society; Professor of Dermatology, University of Kansas. Pp. 207, 115 illustrations. St. Louis: C. V. Mosby Company, 1926. Price, $2.25.

To those of us who, by force of circumstances, must follow tiger trails vicariously, Dr. Sutton offers a delightful excursion to Indo-China and India. The doctor did shoot tigers; he made keen observations of countries and peoples; most important of all: he tells his story in a fascinating way.

R. K.

AN ILLUSTRATED GUIDE TO THE SLIT LAMP. By T. HARRISON BUTLER M.D. Pp. 144, 158 illustrations in text and 5 colored plates. New York: Oxford University Press, American Branch, 1927. Price, $9.00.

FOR beginners as well as for those with experience this book is equally well written and illustrated. It is possibly not so expansive as Koeppe's book, but it so easily readable that those starting slit-lamp work can understand it.

There is an excellent description of the Zeiss slit lamp with diagrams illustrating it.

There are chapters on the cornea, aqueous, lens, posterior lental space and vitreous, which completely cover these subjects.

The diagrams and colored plates clearly amplify the reading matter, making the latter easily comprehended.

It is a book that can be highly recommended to all workers.

H. S.

JUCKENDE HAUTLEIDEN. BY DR. S. JESSNER. 5th edition. Pp. 140. Leipzig: Curt Kabitzsch, 1926.

A WELL-DONE discussion of the diseases, cutaneous and general, in which itching is a prominent symptom. Its popularity is attested to by the need for this, the fifth edition. Among the general diseases in which itching is a symptom, the author fails to allude to Hodgkin's disease and hyperthyroidism.

R. K.

THE PRACTICE OF MEDICINE. BY A. A. STEVENS, A.M., M.D., Professor of Applied Therapeutics in the University of Pennsylvania; Visiting Physician to the Philadelphia General Hospital. Second edition. Pp. 1174; 35 illustrations. Philadelphia: W. B. Saunders Company, 1926. Price, $7.50.

AN excellent book for both the undergraduate student and the general practitioner. Its popularity is attested to by three reprintings and one revision since the original appearance of the work. The text has been thoroughly revised and much new material added. The reviewer is glad to note that references to the literature are found in the footnotes of nearly every page. It should be a means of encouraging students to consult original sources.

R. K.

BOOKS RECEIVED.

Anatomical, Pylogenetical and Clinical Studies on the Central Nervous System. By B. BROUWER M.D. Pp. 67, 16 illustrations, Baltimore: Williams & Wilkins Company, 1927. Price, $2.50. (To be reviewed later.)

L'Angine de Poitrine et L'Angine Abdominale. By D. DANIELOPOLU. Pp. 443, 159 illustrations. Paris: Masson et Cie, 1927. Price, 140 francs. (To be reviewed later.)

Hypotension. Medicine Monograph XIII. By ALFRED FRIEDLÄNDER, M.D. Pp. 216. Baltimore: Williams & Wilkins Company, 1927. Price, $2.50. (To be reviewed later.)

Evolution of Preventive Medicine. By SIR ARTHUR NEWSHOLME, K.C.B., M.D., F.R.C.P. Pp. 226, 6 illustrations. Baltimore: Williams & Wilkins Company, 1927. Price, $3.00. (To be reviewed later.)

The Care of the Patient. By FRANCIS WELD PEABODY, M.D. Pp. 48. Cambridge: Harvard University Press, 1927. Price, $1.00. (To be reviewed later.)

United Fruit Company Medical Department. Fifteenth Annual Report, 1926. Pp. 355, illustrated. Boston: United Fruit Company, 1927.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

JOHN H. MUSSER, M.D.,

PROFESSOR OF MEDICINE, TULANE UNIVERSITY OF LOUISIANA, NEW ORLEANS.

The Relation between the Blood-urea Concentration and the Amount of Functioning Renal Tissue.—Normally the blood urea is subject to considerable variation, depending both upon the rate of urea formation and the rapidity of the rate of excretion. The upper limit of normal, however, is comparatively low just so long as there is a sufficient amount of functioning renal tissue. High blood urea figures in the terminal stages of nephritis are so frequently found that it is well appreciated that this depends upon extensive loss of functioning renal tissue. Just how great this loss of renal tissue must be has not been known. In an attempt to answer the problem, MacKay and MacKay (*J. Clin. Invest.*, 1927, **4**, 127) have studied a series of patients with nephritis. The amount of functioning renal tissue was determined by a method which has been described by Addis, in 1922, and will not be repeated. The authors found that blood-urea concentration did not begin to rise markedly until the active kidney tissue was reduced to about half its original amount. The blood-urea concentration becomes higher and higher as the amount of functioning renal tissue decreases. These observations are of interest and of value if the method of testing the amount of renal tissue is a correct one.

Heart Disease from the Point of View of the Public Health.—In the DeLamar Lecture last fall Cohn (*Am. Heart J.*, 1927, **2**, 386) brought out some very interesting studies which now appear in print. One of the closing paragraphs summarizes so well the problem of heart disease in regard to public health that it will be quoted in full: "It was my intention to show in this very incomplete summary that from

the point of view of the public health, the problem of heart disease is not simple as was that of tuberculosis, but manifold. It included disability incident to the process of aging. The effort to relieve rheumatic fever by removing areas of infection still wants prosecuting before a judgment on its value can be given. To prevent the onset of the disease is still impossible. Theoretically the situation in syphilis is more fortunate; practically the methods of prevention and treatment offer enormous difficulty. Nor has a final conclusion been reached on the value of treatment. There also more knowledge is wanted. The disabilities dependent solely on age, the major aspect of the problem, must elude approach on the side of etiology; to provide relief from distress must be the direction in which to expend effort."

On So-called Gastric Hypertonus and Gastroptosis and Atonic Dilatation of the Stomach.—HURST (*Guy's Hosp. Rept.*, 1927, **77**, 22) discusses with his usual facile pen some observations he has made on so-called gastric hypertonus and gastroptosis. He contends that gastric hypertonus, so-called, practically never exists, and that it is a very open question as to the existence of the average "dropped" stomach. He believes that the two types of stomachs which are so classified should be called "short stomach" and "long stomach." They should be regarded as normal anatomic variations in a stomach of average length.

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY IN THE MEDICAL SCHOOL AND ASSOCIATE PROFESSOR OF SURGERY IN THE SCHOOL FOR GRADUATES IN MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL AND NORTHEASTERN HOSPITALS.

Fractures of Skull.—VANCE (*Arch. Surg.*, 1927, **14**, 1023) says that many patients were admitted to the hospital in a moribund condition or lingered for several days in the hospital, finally dying of suppurative meningitis, pneumonia or sepsis. A series of 61 cases were studied in some detail. They were divided into patients on whom a craniotomy had been performed and patients recovering under expectant treatment. Thirty-four craniotomies were performed; 11 recovered while 27 patients recovered under expectant treatment. Patients treated by craniotomy were subjected to rather rigid physical examination before the procedure was attempted. It was necessary to determine whether there were signs of an intracranial condition that made craniotomy advisable. In the 34 patients operated upon, 3 indications for operating were discovered—compound or depressed fractures of the skull (3 died and 7 recovered); second, in the presence of definite intra-

cranial tension, especially if the lesion causing the trouble could be definitely localized by neurologic examination (20 patients died and 3 recovered); third, with the presence of a disabling paralysis on one side (1 patient recovered). The 27 patients who recovered under expectant treatment were practically over the acute effects of the injury in from twenty to twenty-four days after the trauma. The fracture was located by the Roentgen ray examination in 24 cases, then a compound fracture in 2 instances and by subcutaneous emphysema of the frontal region in 1. The 11 patients who recovered under operation showed a variety of phenomena. Four patients had some definite disability which improved in time, but did not entirely disappear. Most of the 27 patients recovering under expectant treatment did not show any severe after effects except vague symptoms of headache, dizziness and the like.

A Preliminary Study Bearing on the Specific Causative Factors of Multiple Infective Arthritis.—HADJOPOULAS and BURBANK (*J. Bone and Joint Surg.*, 1927, **9**, 278) state that whether these blood culture strains produce symptoms because of exotoxins, and if such be the case, the possibility of creating a satisfactory antitoxin to combat these manifestations are questions which are still being investigated. The experimental work of this present study seem to further emphasize the following theories: (1) That the main primary cause of chronic rheumatoid arthritis seems to be a highly selective group of streptococci; (2) that in the symptom complex of chronic rheumatoid arthritis a secondary rôle may be played by diphtheroid bacilli, bacilli of the paracolon group and Staphylococcus aureus. Some of the diphtheroid bacilli isolated from the blood stream of arthritic patients exhibited such protean properties as to make the authors wonder whether they were not a transition stage between cocci and bacilli.

Infectious Osteomyelitis: Differential Diagnosis.—BROMER (*Am. J. Roentgenol. and Rad. Therap.*, 1927, **17**, 528) reports that pyogenic osteomyelitis will produce a roentgenogram which will usually be diagnosed (without error when it conforms to its usual pathologic manifestations). When it undergoes the destructive stage it probably will not be confused with the other infections, syphilis and tuberculosis, especially when it is accompanied by large and well-defined sequestra. Syphilis will be usually formative and tuberculosis will be largely destructive combined with bone atrophy. The chronic stage of osteomyelitis when the picture is that of a formative process and no evidence of sequestration and involucrum formation can be found is likely to be confused with syphilis and the differentiation depends largely on the history and laboratory findings. Tuberculosis of the shaft, although rare in occurrence, will probably only be differentiated by other means than the Roentgen ray alone. Ewing's tumor or endothelioma of bone is most likely to be confused with osteomyelitis inasmuch as the usual criteria of malignancy are not to be seen. On the history must be placed most dependence. The early stage of periosteal sarcoma cannot always be differentiated because in these cases pyrexia pain and swelling may simulate the signs and symptoms of acute osteomyelitis. Too much dependence must not be placed on the occurrence of perpendicular

striations as a pathognomonic sign of malignancy. These have been noted in cases with acute osteomyelitis and syphilis. Infantile scurvy will cause no difficulty if its early signs are sought for and found on the roentgenogram. Bone cysts will be differentiated with fair degree of accuracy if the signs of pyogenic inflammatory change are recognized. Generalized fibrocystic osteitis should not be so difficult to differentiate from osteomyelitis but presents more difficulty in relation to syphilis.

Hepatitis and its Relation to Cholecystitis.—MARION (*Ann. Surg.*, 1927, **85**, 535) states that one of the main functions of the liver is the destruction and disposal of bacteria and toxic substances. Bacteria and toxic substances reach the liver in a great number of ways and very frequently throughout life. Some are destroyed there without appreciable reaction and all grades of appreciable reaction occur. The morphologic changes which occur in the liver in the reaction of the cells to irritants, and which are called by pathologists hepatitis, are extremely difficult to classify. It is in no sense an entity nor can it be discussed with profit as an entity. Many of the cases formerly grouped under acute catarrhal jaundice are now considered forms of infectious hepatitis. In the forms of hepatitis which have reached the level of clinical observation there is little evidence of a relation to clinical forms of cholecystitis. The hepatitis regularly found with cholecystitis has little or no clinical significance, and is not a factor of importance in causing clinical forms of liver cirrhosis. The proof that very slight infiltration of the gall bladder wall and lipoid deposit in the mucosa cause acid indigestion, a feeling of fullness in the epigastrium, flatulence, intermittent gastric pain after badly prepared food, is by no means conclusive.

Surgical Treatment of Prostatic Abscess.—HALL (*California and Western Med.*, 1927, **26**, 332) says that prostatic abscesses are frequently sequelæ of nongonorrheal infections. Early diagnosis and rational surgical treatment results in less destruction of prostatic tissue and shorter convalescence than palliative measures. Direct vision and dependent drainage of all the abscess cavities is a satisfactory surgical procedure, by U-shaped perineal incision. The best results should be expected when there is the least interference with the normal functions of the bladder, urethra, generative structures and rectum. Following convalescence the resulting prostatitis should be treated as any case of chronic prostatitis. Endoscopic examination of 6 patients operated upon by the author's method showed no distortion of the posterior urethra. Twenty-three were operated upon with ages ranging from fifty-two to eighteen years. The cause of prostatic abscess was found to be nongonorrheal in 8 cases. Three of these nongonorrheal cases were due to trauma; 4 followed pneumonia or influenza; 1 followed furunculosis. Epididymitis was the most frequent postoperative complication.

The Gonophage.—PELOUZE and SCHOFIELD (*J. Urol.*, 1927, **17**, 407) declare that the gonococcus during its process of autolysis produces a substance that is lytic to other gonococci. This gonophage is present in practically all old cultures of gonococci. Undiluted gonophage has

no toxic effect upon white mice when injected in quantities of 2 cc. intraperitoneally. In human beings no toxic effect occurs after the hypodermic injection of 1 cc. The limitation of gonorrheal urethritis to the anterior urethra alone in dispensary patients under oral treatment is a very rare event and almost unknown in the negro. In a series of 40 such patients receiving injections of gonophage, 7 of the infections remained anterior. Three of these 7 were negroes. Such a result would suggest that the gonophage does have some favorable action against the disease in some individuals and that other ways of using it might give better results. The occurrence of systemic and local metastases as well as the presence of gonococci in the urethral and prostatic secretions in some patients long after the administration of gonophage would suggest that it does not greatly affect the body immunity processes. This is as would be expected in a disease that produces no immunity.

Osteomyelitis, Acute and Chronic: A Study of Fifty-eight Cases.— GARR (*Kentucky Med. J.*, 1927, **25**, 80) report 3 cases that refused operation and in 1 with septicemia operation was not advised. Two patients were practically healed when advice was sought and 1 with Brodie's abscess of twenty years' duration went away to think about an operation. In the acute type of the disease 6 patients had septicemia as proven by blood culture. Three of the 6 died following operative intervention and 1 died without operative intervention. Two were cured. The other 14 acute cases were cured or improved on leaving the hospital. Eight patients required a secondary operation. In the chronic type 1 patient died two months after leaving the hospital because of an invasion of the knee joint from the lower extremity of the femur. Amputation was advised in this man, aged seventy years, but it was refused. In 19 cases, or 50 per cent, of the chronic type the author has been able to state a cure was effected. Others drifted away, returned to a distant home or are still under treatment. The mortality of the 58 cases in this series was 12 per cent. The mortality in 51 cases which had operation was 7.8 per cent. Omitting the cases complicated by septicemia, there was but 1 death, which is a mortality of 1.9 per cent. The incidence of sex was 33 males and 25 females, and the right and left sides of the body were equally involved. Only 1 patient was a negro. Fifty-seven whites to 1 of color would indicate that hemotogenous osteomyelitis is another disease to which the negro race is not readily susceptible.

Some Aspects of the Problem of Joint Tuberculosis. — HIBBS (*South. Med. J.*, 1927, **20**, 278) believes that cases must be followed over indefinite periods of time to give trustworthy observations in such important studies, where the course of disease is long and recurrences frequent after many years of apparent quiescence. The author gives the end results of 77 cases of knee joint tuberculosis that were treated at the Country Branch of the New York Orthopedic Hospital, and have been under observation for periods from five to fifteen years. In 13 per cent of these cases an incorrect diagnosis was made. Seven of the remainder died from other forms of tuberculosis. Forty-three of the knees became quiescent and 16 became active again, leaving only

27 inactive cases. This term is used advisedly because it has been found time and again that patients with tuberculosis who were thought to have been cured for many years have had recurrences of the old condition. Of the 27, 5 have stiff joints; 22 have varying degrees of motion but all with marked limitation and seriously crippled joints, so that the final result of the conservative treatment in 33 cases was active disease. Sixteen of them subsequently had a fusion of the knee by operation and have remained free from symptoms. The results in conservative treatment of tuberculosis of the hip are still worse. It would seem inevitable that this study offers convincing evidence that our conception of the cure of joint tuberculosis must be revised and our methods of diagnosis perfected. Moreover there is no evidence yet to prove that heliotherapy has any particular influence upon the progress of the disease and there is grave danger that the belief that it does so, which is so generally accepted, may delay the proper study of this disease for another decade.

Splanchnic Anesthesia.—TAKATS (*Surg., Gynec. and Obst.*, 1927, **44**, 501) states that the terms posterior and anterior splanchnic anesthesia are recommended to take the place of the terms used by various authors. The prevertebral space in front of the first and second lumbar vertebræ is an isthmic point where the sensory fibers of the upper abdominal organs unite to form plexuses. Experimental and clinical evidence show conclusively that the block of the splanchnic nerves on both sides results in an anesthesia of the upper abdominal organs. The lower abdomen can be anesthetized by adding to the splanchnic block the anesthesia of the lumbar rami communicantes. The underlying physiologic principles then which led Kappis first to use splanchnic anesthesia on man was the idea of blocking the splanchnic nerves and rami communicantes at an isthmic point instead of blocking the rami communicantes individually by paravertebral injections from the sixth dorsal to the third lumbar vertebra. The safest dosage of novocain seems to be 70 to 100 cc. of 0.5 per cent solution. In bad risks solutions of 0.25 per cent of the same amount are advisable. The technical part of the problem was to deposit satisfactory amounts of this solution in the prevertebral loose connective tissue before the first lumbar vertebra. The way of approach is either from the back or through the open abdomen. A comparison of the untoward effects and dangers of the two methods as to efficiency shows that the anterior route is superior to the posterior route. Anterior splanchnic anesthesia is indicated in operations for upper abdominal well-localized lesions. The longer the operation is apt to last and the more handicapped the patient is by the degeneration of parenchymatous organs, the more beneficial will be its use.

Cervical Rib.—ADSON and COFFEY (*Ann. Surg.*, 1927, **85**, 839) declare that in about 55 per cent of the cases reviewed in their series, the cervical ribs were symptomless. Patients with cervical ribs without symptoms should not be informed of the accidental finding as this may give rise to neurosis with symptoms referable to the rib. The surgical indications depend directly on the degree and the type of the incapacity produced by the presence of pain, hyperesthesia, anesthesia

and circulatory disturbance. Surgical treatment should not be advised for mild, indefinite pain in the neck and shoulder. The anterior approach and tenotomy of the scalenus-anticus muscle are preferable to the transcervical approach and resection of the cervical rib, since the same relief is offered, the procedure is less formidable and postoperative numbness in the arm and palsy of the brachial plexus are avoided.

Inflammatory Conditions of the Digestive Organs.—Soresi (*Am. J. Surg.*, 1927, **2**, 443) says he can describe anatomic faulty conditions that cause and precede pathologic processes observed in the digestive organs, such as ulcers of the stomach and duodenum, carcinoma of the stomach, pancreatitis, cholecystitis, cholelithiasis, stenosis and obstruction of the intestine, acute and chronic appendicitis and chronic constipation. The stage preceding the gross changes resulting in the formation of ulcers, carcinomas, calculi, perforation, stenosis, etc., is not due primarily to the work of microörganisms. It is due (according to the author) to anatomic defects formed during intrauterine life, the fusion of a portion of the transverse mesocolon with the lesser omentum being the most frequent and most important. The great majority of patients who complain of the usual indefinite digestive disturbances actually suffer on account of the fusion of the mesocolon with the lesser omentum as herein described.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.,

OF PHILADELPHIA.

The Treatment of Lethargic Encephalitis.—Eden and Yates (*Brit Med. J.*, 1927, i, 714) suggest that the infection in epidemic encephalitis is a symbiotic process. In the first place the nasal mucous membrane is injured by one of the catarrhal groups of organism, and subsequently the virus of encephalitis is inhaled, passes through the injured mucous membrane, and thus enters the tissues, reaching the brain possibly by the perineural lymphatics. In support of this there is a fair amount of evidence that for the transmission of the disease from one individual to another the virus of epidemic encephalitis must fall on mucous membrane previously altered by inflammation of such a character that its powers of absorption of fluids in contact with it is greatly increased. The initial injury to the mucous membrane is generally remediable by treatment, and if remedied, it would appear that the virus of encephalitis cannot pass into the tissues. In those cases in which actual destruction has occurred in the central nervous system where regeneration is impossible, the most that can be said for washing out the nasal sinuses is that further irreparable injury is hindered, and in many cases appears to be prevented.

Rickets.—GERSTENBERGER (*J. Am. Med. Assn.*, 1927, **89**, 261) states that in human infants the vitamins do not play a primary part in the development of rickets. If they did, human milk, which is the sole food for infants at a time of their existence when rickets is most likely to develop, should be richer in antirachitic factor than it seemingly is. The fact that cod-liver oil which contains the so-called vitamin D, cures rickets, does not prove that rickets observed in human infants primarily is a vitamin deficiency disease. Cod-liver oil is our civilization's substitute for exposure to sunlight. It seems that nature expects the human skin to be exposed to sunlight in order that the human infant may grow in a physiologic manner. Lack of exercise, especially when enforced by confinement, has been put forth as a primary cause of rickets and yet any amount of exercise will not remove the characteristic pathologic features of rickets in blood and bone. It cannot be a primary factor in the development of rickets in human infants. Heredity cannot contribute in a primary manner to the development or to the lack of development of rickets. No infant of however good stock can escape the development of rickets if he is permitted to grow normally in the complete absence of antirachitic factor. The rickets may be less severe than that found in another infant existing under the same conditions. Such factors as heredity, lack of exercise, cows' and human milk containing diets, and vitamin all play merely secondarily etiological roles to the primary and fundamental cause of rickets which is inadequate exposure to the actinic rays or their equivalent. The amount of exposure or the amount of antirachitic factor in the form of cod-liver oil necessary to prevent rickets seems to bear a direct relationship to the rate of growth. As the rate of growth of an infant usually is greater in the younger infant, his antirachitic factor requirements likewise is greater, and paradoxical as it may seem, the younger the infant, the greater is the amount of cod-liver oil required. It has been found that the actual amount of cod-liver oil required is not more than 1 cc., provided it is commenced before the rickets develops. In order to prevent rickets, the administration of cod-liver oil or the exposure of the child to actinic rays should begin early. The author thinks that the second week of life is not too early. The great primary importance of the actinic ray to normal growth is evidenced by the fact that rickets occurs most severely and most frequently at the end of winter and especially in those infants whose skins are pigmented. In preventing rickets in premature infants it seems necessary in addition to giving an adequate supply of antirachitic factor to increase protein and mineral intake, even when they are getting a maternal supply. This can be readily done by the addition of boiled skimmed milk to the diet. When rickets is prevented there is also prevented the so-called idiopathic tetany or spasmophilia. If rickets has developed and if it is continuously and adequately treated with the antirachitic factor, spasmophilia and tetany will not appear. If the treatment is interrupted as in the irregular sunshine tendency of certain seasons, then the spasmophilic picture will appear.

Studies on Varicella.—MITCHELL and FLETCHER (*J. Am. Med. Assn.*, 1927, **89**, 279) remind us that many adults will develop varicella if exposed to it and if not protected by the immunity of a previous attack. Varicella occurs in young infants and may be congenital if the mother is

suffering from the disease. In their series 775 cases occurred in patients aged from one day to fifty-five years. It was observed that varicella is somewhat more frequent in the winter months. Out of this entire series only 9 gave the history of a previous attack of varicella. Complications were unusual and were nearly always mild, the most frequent being furunculosis and otitis media. There were 2 deaths in the series. One of these was indirectly due to the varicella but the other was due to entirely different cause. The average of the leukocyte counts in 237 counts was increased about 3000 above normal in infants even on the first day of the eruption. The age groups between six and twenty years showed a leukocyte count of about normal on the first day, increasing to about 2000 to 3000 above normal by the third day. There was a very slight increase in leukocytes in adults in the first three days. When studied individually, the number of patients showing leukocytosis or leukopenia in the first three days was about equal. From the fourth to the ninth day the average leukocyte count was about 2000 to 3000 above normal. Minor changes in leukocytes should be interpreted with caution because of the normal daily fluctuation in the count.

Antirachitic Activity of Irradiated Cholesterol, Ergosterol and Allied Substances.—Hess (*J. Am. Med. Assn.*, 1927, **89**, 337) says that the most practical application of an irradiated food is the use of irradiated dried milk for infant feedings. It is the unanimous opinion that dried milk treated in this way prevents or cures infantile rickets and tetany. The specific activity of the milk is maintained for a period of at least six months. Irradiated cholesterol has been successfully used as an antirachitic. This may be added to cod-liver oil to increase its potency. Dried brain, which contains an exceptionally large amount of cholesterol has been irradiated and used with success. It has been shown that it is not the cholesterol itself which undergoes activation, but probably a contaminating sterol intimately associated with it. Among a large number of sterols which were irradiated and tested for antirachitic power it was found that ergosterol was the only one which acquired antirachitic power. This sterol, which is prepared from yeast, brought about the calcification of the epiphyses experimentally when as little as 0.002 mg. was fed daily. This is the smallest amount of any of the nutritional factors or vitamins which has been found to exert a specific action. Instead of ergosterol, irradiated yeast may be employed as an antirachitic. This product has been highly effective in animals and infants.

Purpura Hemorrhagica.—Tolstoi (*J. Am. Med. Assn.*, 1927, **89**, 370) treated 3 cases, using the mercury-vapor quartz lamp. The results were not satisfactory. He points out that recovery occurs at times without any treatment, so that it is obvious that the evaluation of any new therapeutic measure is exceedingly difficult, and before such a method is accepted, it must conclusively prove that it alone has produced the result. There are cases on record in which the patients have been symptom free for years only to have recurrences later. Because of the knowledge that patients often recover spontaneously, the treatment in the mild cases has been expectant and hygienic, while in the more

severe ones transfusion has been the choice method of therapy. It was observed that although many persons recovered, a group failed to improve, and deaths occurred in spite of repeated transfusions. Lacking a better means of treatment than transfusion, splenectomy was advocated and the results in the literature certainly indicate that this is advantageous in cases of essential thrombocytopenia. Other methods of treatment have been used. One of these is the Roentgen ray treatment of the ovaries upon the assumption that some ovarian dysfunction exists as most of the patients are females. Others have advocated Roentgen ray treatment of the spleen.

Some Observations Regarding Diphtheria Immunity.—KELLOGG and STEVENS (*J. Am. Med. Assn.*, 1927, **89**, 273) indicate that the Schick test and the guinea-pig test for diphtheria immunity give parallel results in primary tests. In persons who have been immunized with toxin-antitoxin and a negative Schick test obtained, some show no antitoxin by the Kellogg method. In the writers' series this occurred in from 20 to 25 per cent of the cases. Most of these show traces when tested for small amounts by the Romer method, but a few do not show any at all. These persons are latently immune, because they quickly develop antitoxin in titratable amounts if given a secondary stimulus in the form of a single injection of toxin-antitoxin and at times even as small a stimulus as the Schick test will stir up antitoxic reaction. There is an essential difference in the permanence of the free antitoxin in the circulating blood of the naturally immune and of those artificially immunized. This difference together with the fact that the naturally immune as shown by the Schick test always have free antitoxin while the artificially immune do not always have it, suggests that natural immunity may not exist solely by reason of exposure to infection but may be in part at least a physiologic process.

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA,

AND

FRANK B. BLOCK, M.D.,

INSTRUCTOR IN GYNECOLOGY, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Parathyroid Extract for Menorrhagia.—It has been shown experimentally that the use of parathyroid extract will raise the blood calcium and increase the viscosity of the blood. The clinical possibilities of such information influenced ALLEN, COMPERE and AUSTIN (*Am. J. Obst. and Gynec.*, 1927, **13**, 156) to investigate the use of the extract to control the bleeding associated with the condition usually known as idiopathic menstrual bleeding. In these cases, no pathologic lesions are found

but the bleeding is sometimes so profuse and resistant to medical means that either surgery or irradiation must be considered. Although their results in this work cannot be taken as conclusive, they are at least suggestive of the possibilities of the parathyroid hormone if used in the optimum dosage and at the proper time. They used comparatively small doses of the extract in the beginning and by gradually increasing the amounts, have endeavored to establish a minimal dose that can be used with satisfactory clinical results. At present they are inclined to recommend a total dosage of from 120 to 160 units, given in divided doses of 20 units, morning and evening. The best results were obtained by starting the intramuscular injection the day before the period was due. From their work thus far they are of the opinion that by the use of the extract of parathyroid gland the bleeding time and clotting time of the blood were definitely shortened. The number of days of menstrual bleeding as well as the amount of blood lost was appreciably reduced and during the intermenstrual period the patients were not so reduced in strength and vitality.

Uterine Cancer in Jewish Women.—In an effort to determine the incidence of cancer of the uterus in Jewish women as opposed to its incidence in Gentiles, HORWITZ (*Surg., Gynec. and Obst.*, 1927, **44**, 355) made an interesting statistical study. Of 1237 cases of primary carcinoma of the uterus seen at the Mayo Clinic between 1920 and 1925 inclusive, 1227 were among Gentiles and 10 were among Jewesses. Ninety-seven per cent of the 1227 patients were married. There was a slightly higher birth rate among the Jewish patients but the difference between the birth rate among Jews and Gentiles was too small to warrant conclusions. From data obtained at the Curie Hospital, where two-thirds of the patients were treated for carcinoma by Roentgen rays or radium, the incidence of carcinoma was slightly less for Jewish patients as compared with carcinoma in Gentiles. In general he has found that carcinoma of the uterus is comparatively infrequent among Jewesses, being about one-fourth as frequent as in the Gentile women (3.9 per cent as compared with 16.5 per cent). Carcinoma of the breast is common among Jewesses and almost equals the percentage in Gentile women, while cancer of the digestive tract, including the liver and pancreas, was almost twice as frequent in the Jew as in the Gentile. Some of the reasons advanced to explain the relative infrequency of carcinoma of the uterus in Jewish women are racial immunity, the ritual dietary laws, poverty and the more normal blood supply to the generative organs in the Jewess. These and many other reasons, however, have been refuted by other authorities. The fact still remains that in spite of the fertility and longevity of Jewish women, carcinoma of the uterus is relatively infrequent among them.

Experimental Irradiation of Tumors.—The clinical treatment of tumors by irradiation brings out two outstanding facts; first, there are wide differences in the sensibility of tumors of different kinds and second, that tumors of the same kind in different patients also vary in sensibility, though the variations are less wide than when tumors of different kinds are compared. The first kind of variation has been considered to reside in the tumor cells, but when different kinds of

tumor cells are irradiated *in vitro* the lethal dose is found to vary very little. The second kind of variation must reside in the patient and has been assumed to be due to a resistance toward tumor growth, which varies from patient to patient. It is evident that there are no certain explanations for these two important clinical facts and in order to elucidate them MOTTRAM (*Brit. Med. J.*, 1927, i, 275) performed some experiments on mice which showed that tumors left for from four to five days in the animal after irradiation, and then removed and grafted into other animals, succumb more easily than when removed immediately after exposure. This effect is associated with an interference with the blood supply, which occurs from four to five days after the exposure. These results suggest that the varying sensibility to irradiation of tumors, and the difference in sensibility between normal tissues and tumors, are associated with the variations in blood supply on which the irradiation has a special action apart from its direct action on cells.

OPHTHALMOLOGY

UNDER THE CHARGE OF

WILLIAM L. BENEDICT, M.D.,

HEAD OF THE SCHOOL OF OPHTHALMOLOGY, MAYO CLINIC, ROCHESTER, MINN.

Optic Neuritis as a Complication of Whooping Cough.—HOGG (*Med. J. Australia*, 1927, **1**, 825–826) reports that, in 6 recorded cases quoted from literature, 2 patients became affected by neuritis in two to four weeks after the appearance of whooping cough; 2 patients became affected after several weeks; 1 after some months; and in the sixth patient brain trouble supervened in the third month, to be followed later by optic neuritis. In the writer's case the eyes became affected in the earliest stage of the disease and optic neuritis was present before the whoop was heard. There was no meningitis or brain complications, nor could mechanical influences be advanced as possible causal factors. The neuritis was apparently due to the action of the toxin or toxins of the germ of the disease.

Interstitial Keratitis.—LAGRANGE (*Franco-British Med. Rev.*, 1927, **3**, 244–247) states that this disease was first clearly differentiated by Hutchinson in 1857, on the strength of numerous clinical observations, as due to heredosyphilis. He attached particular importance to three main features of the disease; interstitual keratitis, deafness, and peculiarities of the teeth. There are three stages of interstitial keratitis. The first is a stage of infiltration when the cornea becomes grayish and assumes the characteristic aspect of ground glass. It usually begins at the center, more rarely at the periphery, but in either case the whole surface is sooner or later involved. This stage of infiltration lasts two or three months. In the second stage of vascularization, some of the

vessels are conjunctival and some are deeply seated, the latter running between the layers of the cornea, eating up the infiltrated leukocytes and restoring its transparency. The more intense the vascularization, the better is the chance of complete absorption. This stage lasts two or three months, if treatment is successful. Following this comes the third stage of absorption, in which the cornea slowly clears and the newly formed vessels gradually become absorbed. The average duration of the disease is one year. It usually begins in one eye but always the second eye is attacked, where the same course is run as in the eye first attacked. Tuberculosis has its own special form of interstitial keratitis, which presents the closest resemblance to the heredosyphilitic type. It can be differentiated by remarking that the cornea is not uniformly infiltrated, but presents opacities of variable size, genuine tubercles, separated by normal surfaces. At a more advanced stage there is no tendency to vascularization, or it is but slight. The course, too, is different. Instead of stages of retrogression and repair, it culminates in necrosis and ulceration, so that it is a grave form of interstitial keratitis. Other varieties of keratitis that may be confused with interstitial keratitis are found in malaria, rheumatism, typhoid fever, diphtheria, pneumonia and influenza.

RADIOLOGY

UNDER THE CHARGE OF

ALBERT MILLER, M.D.,

AND

CHARLES G. SUTHERLAND, M.D.,

CONSULTING PHYSICIANS, SECTION OF ROENTGENOLOGY, MAYO CLINIC, ROCHESTER, MINN.

Roentgenologic Examination of the Bladder.—REISER (*Fortschritte a. d. Gebiete d. Roentgenstrahlen*, 1927, **35**, 756) insists that the bladder should be examined roentgenscopically with a small amount of contrast medium for the detection of lesions. He finds it preferable, after the bladder is completely emptied, to inject 20 or 30 cm. of 20 per cent iodopin with an equal amount of air. In the sagittal, lateral and oblique roentgenoscopic views lesions, however small, are demonstrable, even in corpulent patients. Examination should be made both in the standing and lying positions. Iodopin is not irritating to the bladder, and the method is applicable in the diagnosis of prostatic hypertrophy, diverticula, foreign bodies, tumors, calculi and fistulæ.

Radiotherapy in Hodgkin's Disease and Lymphosarcoma.—DESJARDINES (*Am. J. Roentgenol. and Rad. Ther.*, 1927, **17**) describes 4 cases in detail. The only form of treatment which has shown itself to be really useful is radiotherapy. Judging from case reports the disease remains as incurable as ever, but many patients are relieved for more or less

prolonged periods, and the immediate results are often little short of miraculous. Desjardins prefers to inaugurate treatment with moderate voltages, and he considers it wiser to make the treatment fairly general by directing it not only to such nodes as may be palpable, but also to the mediastinal and lower paravertebral lymph chains.

Hunger Pain.—By means of a single air-filled balloon introduced into the fasting stomach, MARTIN and ROGERS (*Am. J. Roentgenol. and Rad. Ther.*, 1927, **17**, 222) have made roentgenograms which throw some light on the phenomenon of hunger pain. From these findings it would appear that the primary or essential element in the painful hunger contraction appears to be a complete circular constriction in the lower third of the stomach, near the junction of the media and antrum. Contractions in the upper stomach may or may not occur simultaneously. During the period of incomplete gastric tetanus which may occur, there may be, in addition to antral constriction, a general shortening of the stomach and waves suggesting peristaltic activity.

Pulmonary Markings in the Roentgenogram.—Not infrequently exaggeration of the pulmonary markings and mottling of the lung picture due to vascular stasis is misinterpreted as disease of the lungs. In such cases the bronchovascular markings are broadened, intensified and extend to the periphery, and are interspersed with fine or coarse, discrete or confluent flecks. WIERIG (*Fortschritte a. d. Gebiete der Roentgenstrahlen*, 1927, **35**, 704) describes among others a case in which the patient had an endocarditis, and the resulting flecks in the roentgenogram led to a wrong diagnosis of miliary tuberculosis.

Role of Iliolumbar Ligaments in Low-back Strains.—LEUMAN (*J. Am. Med. Assn.*, 1926, **87**, 1002) describes a point of tenderness in the small triangular space formed by the midline of the last two lumbar vertebræ and the posterior portion of the iliac crest found in many cases of back strain. It is common in those whose occupations require frequent rotation of the column, such as shovelling or running, hoisting machinery and in playing golf. It is especially marked along the line of the iliolumbar ligaments in one or both sides and worse at the point of attachment of this ligament to the ilium. It occurs particularly in patients with loose sacroiliac joints, spondylolisthesis, and in patients in whom the Roentgen ray demonstrates one or both sacrolumbar interarticular processes to be crescentic or flattened. Roentgenographically, they show periostitis, production of roughening and occasional spur-formation as evidence of marked increase in pull on the iliolumbar ligaments at the point of their insertion to the crest and lateral processes. Partial or complete calcification of this ligament has been seen, and structural changes in the lateral processes of the fifth lumbar vertebra noted. In the discussion the normal variation of this region was stressed.

Chronic Experimental Ulcer of the Stomach.—WOLFER (*J. Am. Med. Assn.*, 1926, **87**, 725) summarized that the ulcer is the only invariable known factor in the study of peptic ulcer. This specific anatomic and physiologic factor can be produced in the experimental animal. The

experimental ulcer does not cause hyperacidity or hypersecretion in the dog; when the ulcer is near the pylorus there is a definite delay in the emptying time of the stomach, but if it is some distance from the pylorus there is no delay, and a comparative study indicates that the psychic factor in man plays a distinct role in the production of perverted function in peptic ulcer. Judd, in discussion, reviewed Mann's production of ulcers in the duodenum by drainage of bile and pancreatic juice and duodenal secretions into the lower intestinal tract. Then with unchanged gastric secretions going directly into the jejunum true chronic ulcers were produced. Surgeons have had an idea that an ulcer situated into the body on the lesser curvature frequently interferes with gastric motility. If the rhythm of peristaltic contraction is broken on the lesser curvature, the stomach is unable to empty, so in exercising ulcers on the lesser curvature an accompanying gastroenterostomy should be made always.

Roentgenotherapy of Exudative Iritis.—SAMUEL *et al.* (*J. Am. Med. Assn.*, 1926, **87**, 1033) rayed the eye for a foreign body in 1 case of supposedly exudative iritis and a rapid disappearance of the fibrous exudate occurred. Continued experience brought similar results in exudative iritis. A light stimulating dose was given. In the discussion, other observers reported similar good results in radiotherapy of the eye.

Diverticulitis of the Colon, with Especial Attention to the Diagnosis.—ENFIELD (*Radiology*, 1926, **7**, 371) asserts that colonic diverticula are false and acquired; they involve only the mucosa and serosa, the former being herniated through an opening in the muscularis. There is inflammatory thickening due to round-cell infiltration between the two layers and adhesive peritonitis outside the diverticula which have suffered repeated attacks of subacute inflammation. The inflammatory thickening may become extreme and cause a mass which might be mistaken for carcinoma. The sigmoid is most frequently involved and the condition commonest in overweight males over forty, with a history of chronic and more than ordinarily severe constipation. There is a definite group of cases in which carcinoma is apparently implanted in old diverticulosis. Except in the acute attack, the diagnosis depends on the Roentgen ray examination for finality. The "saw-tooth sigmoid," probably due to spasticity, is highly suggestive; the visualization of the diverticula with the use of the barium enema, and of the barium-filled diverticula after the bowel has been emptied, constitute the roentgenologic picture. Right-sided diverticula may give symptoms simulating cholecystic disease; diverticula in the sigmoid may suggest appendicitis. The treatment of acute diverticulitis with abscess formation or with any of the late complications is chiefly surgical. Medical treatment should include: avoidance of severe laxatives, large weekly or biweekly doses of bismuth or barium, injection of 10 per cent solutions of gelatin at a temperature of 120° F., and the use of antispasmodics, of which luminal has been the most successful. Frequent small doses of mineral oil, the administration of bariumized buttermilk every three or four days and a diet of large amounts of coarse vegetables all have therapeutic value.

The Roentgen Treatment of Leukemias.—JENKINSON (*Radiology*, 1926, **7**, 379) divides the leukemias into two main groups, namely, those of lymphadenoid origin and those of myeloid origin. A study of the blood determines the tissues of the body involved. In the average hospital practice the disease averages 2 cases per thousand in incidence, is usually chronic and occurs most often during middle life. It occurs in all parts of the world, affects animals as well as human beings, and very little is known about the etiology. In the Roentgen treatment of chronic leukemias the results have been very good; the rays produce a temporary feeling of well-being, and there is a great increase in the number of working days. He ascribes little importance to the direct treatment of the spleen; the first treatment is over the anterior chest, trying to avoid the spleen. With the daily count diminishing, treatment is withheld. With commencing increase, treatment is continued. After three or four treatments the patient is sent home and returns one day each week for a blood count. Results are better and reactions less severe in cases treated over the chest than in those treated over the abdomen.

Roentgenologic Exploration of Spinal and Cerebral Spaces, Genito-urinary Organs and Other Organic Cavities with Iodized Oil.— SICARD and FORESTIER (*Radiology*, 1926, **7**, 385) first describe the substance lipiodol, a definite chemical compound in which 40 per cent iodin is bound to a fat body, and then enumerate its roentgenologic uses. All samples of brownish color or dim appearance, containing free iodin, must be strictly avoided. Exploration of the epidural space, between the spinal theca and the spine itself, is of great interest in all bony diseases of the spine. In cases of pathologic obstruction, the lipiodol will not flow and a roentgenogram will show the limit of its course. The method has given most practical results in the exploration of the subarachnoid space, rendering possible an early diagnosis and accurate localization of spinal-cord compressions. Points relative to indication, technique and interpretation are emphasized. A preparation of lipiodol with olive oil (light lipiodol) which ascends along the spinal cord within two to three hours to the cerebral ventricles has assisted in the localization of brain tumors. Lipiodol has been used successfully in the outlining of cold abscesses, visualization of the male urethra; the seminal vesicles and the vas deferens; the uterus and Fallopian tubes in the female; the facial sinuses, lachrymal ducts and the salivary glands. The substance has a value in intra-arterial injections of gangrenous extremities, in the study of gastric secretion and activity, in the study of bones and joints, and in animal experimentation.

The Thymus in the Newborn and Early Infancy.—NOBACK (*Radiology*, 1926, **7**, 416) laid particular stress on the posterior projections in extension of the thymus substance. The outline of the thymus in the late fetus and in the still-born child is similar to that described by many roentgenologists as "enlarged" or "hypertrophied." It is quite probable that some thymus may retain this broad type for several years and yet not be pathologic. Other observers failed to find any points of differentiation between the Roentgen ray shadows found in patients with clinical symptoms of enlarged thymus and the shadow in normal

infants. A shadow suggesting abnormal thymic enlargement in 40 to 50 per cent of different groups of normal infants is on record, and the thymus shadow may vary in the same infant at different periods in the first year without any clinical evidence of disease. A definite fluctuation in size of the thymus synchronous with respiration has been noted. Chamberlain, in discussion, stressed the value of the routine lateral ray in the infant to become familiar with the normal. Roentgenographs should be made with the patient in the erect position and just after the inspiratory crow which marks the reopening of the glottis in the crying child. Very slight degrees of backward displacement of the trachea are a definite index of significant thymic enlargement.

The Reliability of Cholecystography by the Oral Method.—STEWART and RYAN (*Am. J. Roentgenol. and Rad. Ther.*, 1926, **16**, 234) defend the oral method of administration in a report of 100 consecutive cases. From this analysis and experience with 400 cases the findings following the oral administration of the dye compare favorably with those obtained from the intravenous method. They give a fatty meal the night before administration of the test, to empty the gall bladder. The use of the fresh drug is emphasized. No fluids or food are allowed until sixteen hours after the dye is taken. A diagnosis of cholecystitis made on a "faint shadow" is of importance only when associated with other direct or indirect evidence of pathology.

Measurement of the Liver by Means of the Roentgen Rays.—PFAHLER (*Am. J. Roentgenol. and Rad. Therap.*, 1926, **16**, 558) has made measurements of the liver in 502 subjects. The average length of the right lobe is 21.3 cm. and the average thickness is 12.8 cm. Sex, age, height, weight and abdominal thickness individually cause little difference in the size of the liver, but a larger patient is likely to have a larger liver than that of a smaller person.

Cancer of the Stomach.—Cancer of the stomach can be cured by the removal of the growth in an early stage of the disease. This must be the keynote of any campaign to lessen the number of deaths from this disease, says BALFOUR (*Surg., Gynec. and Obst.*, 1927, **44**, 103). Cancer of the stomach may exist without pain, without indigestion, without loss of appetite, without loss of weight and without anemia. Examination by the Roentgen ray is now more important than all other methods of detecting this disease. It is safe to say it is the greatest contribution which has been made to the earlier diagnosis of cancer of the stomach. Public instructors should urge the inclusion of a fluoroscopic examination by a competent roentgenologist in the investigation of any digestive disturbance after the age of thirty-five years. When it has been demonstrated by Roentgen ray that a lesion is present in the stomach there are three chances out of four that it is cancer. Ulcer of the stomach not only may be a precursor of cancer but may actually be a cancer at the time it is depicted by the Roentgen ray.

Bone Changes in Congenital Syphilis.—LINDSAY, RICE and SELINGER (*Am. J. Syph.*, 1927, **11**, 128) report on 94 cases of congenital lues in which Roentgen ray examinations were made. The ages of the

patients varied from a few weeks to thirteen years; the youngest was one week old. Eighty-five per cent of the cases with definite lesions of the osseous system were in patients under one year of age. The large bones particularly were affected, and since the shafts are so much more frequently involved than the epiphysis, the chief confusing factor, rickets, can be easily excluded. The tibia was most commonly affected. Changes in the osseous system may be divided into two groups, those with changes occurring early and those occurring late. The early changes in the order of their frequency are: (1) Periostitis; (2) destructive lesions; (3) osteitis and periostitis; (4) osteochondritis; (5) dactylitis. The late changes in order of frequency are: (1) Osteitis; (2) periarticular infiltration. More than one type of lesion often occurs in the same patient and often in the same bone. In the early changes seen in the bones multiple involvement is the rule. The bone lesions which occur early are, as a rule, not permanent and in a comparatively short time are well; this applies chiefly to the periosteal proliferation; the destructive lesions do not heal so readily. Those lesions which occur late, chiefly osteitis, are almost never influenced by treatment. Productive periostitis, destructive lesions at the head of the bone, with or without involvement of the articular surfaces, osteochondritis, with widening of the epiphyseal junction, and irregularity of the line of contact between the epiphysis and the shaft, and dactylitis are also late changes. The saber shin is the most common late manifestation. Periarticular infiltration, usually showing an increased density of the soft parts, is most common in the knee, the hip and ankle, and other joints may be affected. There are quite frequently definite and characteristic changes in the bones of the head; these are not so easily discernible by the Roentgen method.

Massive (Atelectatic) Collapse of the Lung, with Especial Reference to Treatment.—SANTE (*J. Am. Med. Assn.*, 1927, **88**, 1539) accepts Bradford's definition that this is a condition in which the lung, without the presence of any gross lesion, such as bronchial obstruction, pleural effusion, etc., interfering with the free entry of air, becomes airless to a greater or less degree. The condition was first reported by Pasteur, in connection with postdiphtheritic paralysis of the diaphragm. It has been contrasted with the scattered lobular atelectasis that follows obstruction of the bronchioles by secretion or foreign material. It occurs as a postoperative complication of abdominal operations, or following trauma. Commonly the respiratory symptoms predominate, with sudden onset, pain in the chest, dyspnea and rapid pulse. Cyanosis may or may not be present. Fever is at first slight, but may reach 102° F. or higher later. The sputum is scarce at the onset, later becomes more profuse and mucopurulent. It is never bloody or of the prune-juice type. The white cell count is ordinarily somewhat higher than normal. The associated symptoms may completely overshadow the chest condition and the atelectatic condition of the lung is discovered only as an incidental observation. In such cases there may be little or no embarrassment of respiration, or change in pulse rate or temperature. The duration is usually from one to three weeks. The condition may terminate rapidly by sudden reinflation of the lung and reëstablishment of respiratory function, or may require several weeks;

it seldom ends fatally. Postmortem examination shows a state of massive atelectasis and microscopically the walls of the bronchioles and alveoli are collapsed, producing a solidification of the lung structure Radiographically the lung is denser; there is no pneumothorax; the chest wall is depressed; the heart and mediastinal structures are drawn over toward the involved side and the diaphragm is elevated. Reinflation of the lung follows rolling of the patient back and forth on the uninvolved side and the mediastinal structures assume their normal position. The author doubts the mucus plug as an etiologic factor and has found the rolling more rapid and more universally successful than bronchoscopy or other methods of treatment.

The Radiographic Signs of Pulmonary Insufficiency.—At 6 feet the Roentgen ray plate of a normal heart presents on the left border from above downward the aortic knob, the left auricular appendix and the ventricle. In uncomplicated cases of mitral stenosis, with enlargement of the left auricle, right ventricle and the pulmonary conus, states SCHWARTZ (*Am. Heart J.*, 1927, **2**, 407), there is a tendency for the heart to rotate to the left as well as backward and upward. The left border then, in the usual cases, presents from above downward a very small aortic knob, a slightly dilated pulmonary artery, a prominent left auricular salient (pulmonary conus plus the auricular appendix) and the enlarged left ventricle, especially when mitral insufficiency has been present for some time. The predominating bulge in these cases is usually immediately above the left ventricle, supposedly involving the lower portion of the left auricular salient. Cases of severe mitral stenosis show, as a rule, an increase in the left auricular salient as a characteristic feature of this condition. The pulmonary artery, excepin children, with mitral stenosis, is slightly dilated. In cases complit cated by pulmonic insufficiency, however, the pulmonary artery is widely dilated and shows so in the roentgenographic film. Fluoroscopically, cases with mitral stenosis, when placed in the right anterior oblique position, show as a characteristic sign of the disease a marked encroachment of the left auricle upon the retrocardial space. This is true also in cases where there has been an accompanying mitral insufficiency of long duration, so as to cause left ventricular hypertrophy. With the patient in the same position, there is only moderate bulging of the pulmonary artery visible in the uppermost part of the cardiac shadow toward the anterior part of the chest. In the cases of mitral stenosis, however, which present a diastolic murmur at the second or third intercostal spaces to the left of the sternum (in the absence of aortic disease) the pulmonary artery almost assumes the first upper curve of the left side of the heart in the form of a huge bulge which shows just as prominently in the right anterior oblique position. The artery does not pulsate forcibly, as in congenital lesions of the heart. When the left ventricle is not markedly enlarged this pulmonic bulge may also be seen in the uppermost space adjacent to the spinal column, with the patient in the left posterior oblique position. The roentgenograms of cases with mitral stenosis accompanied by pulmonic insufficiency simulate very closely those of congenital lesions of the heart, such as patent ductus arteriosus, pulmonic stenosis and ventricular septal defects. The electrocardiographic tracings correspond with the roentgenologic findings.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY, UNIVERSITY OF TORONTO, TORONTO, CANADA,

AND

W. L. HOLMAN, M.D.,

ASSOCIATE PROFESSOR OF BACTERIOLOGY, UNIVERSITY OF TORONTO, TORONTO, CANADA.

Metastatic or Embolic Endometriosis.—Some years ago SAMSON (*Am. J. Path.*, 1927, **3**, 93) demonstrated the possibility of the entrance of foreign material into the venous channels opening on the endometrium of the uterus during menstruation or after curettage. He has since made a careful study of the venous and lymphatic circulation in the uterine wall. On a previous occasion he has demonstrated the presence of endometrial implants upon the peritoneal surface of the pelvic organs and the evidence appears to be quite conclusive that the implants were the result of the regurgitation of small endometrial fragments arising at the menstrual period. In the present communication Samson attempts to explain the mode of origin of endometrial implants in the uterine wall. These studies were carried out upon uteri removed during menstrual cycle, and from his analyses he arrives at the conclusion that small portions of uterine mucosa sometimes escape into the venous circulation of the uterus. Furthermore he has been able to show, that some of these endometrial masses implant themselves upon the walls of these vessels, giving rise to a small focus of glandular tissue similar to that lining the uterine cavity. These small islands of endometrial tissue remain living and grow, passing through the tissue reactions during menstruation like those of normal endometrium.

Essential Adrenal Insufficiency.—Idiopathic adrenal insufficiency with the Addisonian syndrome does not occur very commonly. In the majority of instances adrenal insufficiency has been associated with the presence of pathologic processes such as tuberculosis and tumors, destroying both adrenal glands. There are however, a certain number of cases in which no such disturbing factors can be demonstrated. In this latter group MEDLAR (*Am. J. Path.*, 1927, **3**, 135) found that both sexes were almost equally involved and the clinical manifestations made their appearance at almost any decade in life. In these cases it is noted, that a status thymicolymphaticus is not uncommonly present with the Addison's syndrome. The association of changes in these various ductless glands occurs in sufficient frequency to impress one with the importance of the interrelationships between the various endocrin secretions. The Addisonian syndrome is produced only in cases of extreme adrenal insufficiency and the status lymphaticus is but an indication of the disfunction of the adrenal. Nothing is known of the factors causing the adrenal disturbance in these cases.

Pyorrhea Alveolaris: the Role of Certain Microörganisms Found in Lesions.—FISHER (*Am. J. Path.*, 1927, **3**, 169) has again studied the flora of the mouth in health and disease. By carrying out a careful technique he has been able to determine the varying flora, which occur about the gums and particularly those, which are associated with the presence of pyorrhea. In them he found that the amœba could be demonstrated in 95 per cent of the exudates and associated with these microörganisms the B. fusiformis was always to be found. Some variety of the Streptococcus viridans was present about the gums and the pyorrheal sac in every case, in which the disease was manifest, while these organisms were only occasionally present upon the gums of normal individuals. More striking than this, however, it was noted that the viridans organism normally present in the mouth was the Streptococcus salivarius, while in those possessing pyorrhea the Streptococcus mitis was the common organism of the infection.

Fat Content of the Normal Human Thyroid.—The presence of fat in the epithelial cells and within the colloid substance of the thyroid has been commented upon by several authors. No attention however has been given to the question whether this fatty material was the outcome of processes of degeneration or resulted from secretory activity. JAFFÉ (*Arch. Path.*, 1927, **3**, 955) studied 70 thyroids from individuals varying in age from one day to eighty-six years. Only fresh and apparently normal glands were used. He observed that fat droplets were present in the human thyroid from the first year of life and that these increased with advancing age. This fatty material was present along the borders of the epithelial cells as well as within the colloid material itself. He found that the lipoid droplets in the epithelium are the product of secretory activity and by means of staining reactions he found that they consisted of mixtures of phospholipins. These lipoid substances are secreted into the acinus to become mixed with the colloid content. The rate of excretion and to some extent the character of lipoid substance changes under pathologic states. The author also believes that some of the lipoid substance is extruded into the stroma where it is taken up by the histiocytes.

So-called Chronic Appendicitis.—During the last decade or two the term chronic appendicitis has been applied to a great number of fibrosing lesions in the appendix in which no indication of an antecedent inflammatory process could be determined. Furthermore it has been found that chronic appendicitis in the clinical sense is not uncommonly associated with manifestations in other portions of the gastrointestinal tract. RHODENBURG (*Arch. Path.*, 1927, **3**, 947) examined 3214 appendices among which 1347 were diagnosed as productive appendicitis or what is otherwise spoken of as chronic appendicitis. These productive lesions begin at the tip and gradually proceed toward the cecum. The author found that the first changes were observed in the presence of a group of cells surrounding Meissner's ganglion. This reaction is slowly followed by fibrosis which extends into the neighboring tissues. In the final stage the involved ganglion is found to be embedded in dense scar tissue which distorts it. He found that this reaction was confined to Meissner's ganglion and did not involve the Auerbach's nodes.

As the fibrosis progressed, a thickening of the serosa may take place and sclerosis of the bloodvessels is not uncommon. The author believes that chronic appendicitis is a productive inflammation of the localized nodes of the sympathetic nervous system. The lesion is not confined to the appendix as it is also found in the gall bladder and other portions of the gastrointestinal tract. He suggests that this offers an explanation for the protean clinical manifestations.

Pulmonary Embolism.—McCartney (*Arch. Path.*, 1927, **3**, 921) analyzed 73 cases of fatal pulmonary embolism observed in 9275 autopsies performed at the University of Minnesota. These cases he divided into four groups: (1) Posttraumatic, 23; (2) postoperative, 31; (3) postpartum, 3; and (4) medical, 16 cases. Of these there were 40 males and 33 females, the age varied from nineteen to eighty-three years. From his analysis of the 23 posttraumatic cases and 119 reported in the literature, the author concludes that thrombosis and embolism are not rare, and occur more commonly after simple fractures than in association with compound fractures. In a number of instances there was only bruising of the soft tissues without the fracture of a bone. He finds that a thrombus always developed at the site of the injury, and the interval of time between the trauma and the pulmonary embolism is longer than when pulmonary embolism arises after operation. Injuries resulting in embolism involve the lower extremities more frequently than the upper. In the postoperative group of 31 cases, wound infection was present in 17, and in 27 of them the embolism appeared during the first two weeks. The primary site of the thrombosis may lie within the operative field or be distantly removed from it. The iliac, femoral and pelvic veins, particularly on the left side are the most common site of the primary thrombosis. Postoperative pulmonary embolism only follows operations below the diaphragm, and particularly following operations on the prostate, intestine, and biliary tracts. Thrombosis and embolism develop in a great variety of medical conditions and the primary lesion is found in the lower extremities often independent of the important anatomic lesions.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE, WASHINGTON, D. C.

What-price Smallpox.—Chapin (*Public Health Reports*, 1926, **41**, 2788–2790) asserts that in the last fifteen years the United States has had over 700,000 cases of smallpox reported, which is more than any

reporting country excepting only India, and possibly Mexico. Over 100,000 cases were reported in 1921 in this country. Chapin argues that vaccination is much preferable to even a mild attack of smallpox and scouts the idea that the old-fashioned severe type is extinct, pointing to the 163 deaths in Detroit, to 363 in Minneapolis, 20 in Washington, D. C., and 136 in Los Angeles in support of his statement. The argument for vaccination in the final paragraphs is: "When there is no smallpox-people say 'Why should we worry? Why should we be vaccinated?' That is what the 136 Los Angeles victims said last year. Now it is too late. How many people are saying the same thing this year? What price will they pay? Intelligence and vaccination, or indifference and smallpox? Every physician and every board of health is ready to vaccinate you now, before it is too late. Have you consulted them as yet? If not, do it now."

Benzol Poisoning as an Industrial Hazard.—GREENBURG (*Public Health Reports*, 1926, **41**, 1357) treats acute *benzol poisoning* in two groups, cases in which there is a direct toxic action and cases in which there is asphyxiation due to exclusion of air. The rather meager reports of the period prior to the World War are reviewed briefly, and full consideration is given to the more recent experience. The general symptoms and treatment are given as follows: In general, the symptoms and signs of acute poisoning by inhalation are faintness, dizziness, excitation, pallor and later flushing, weakness, headache, breathlessness, apprehension of death, tightness in the chest, visual disturbances, tremor, weakness in extremities, rapid pulse, cyanosis, unconsciousness or narcosis, collapse, tremor and convulsions, coma, acute mania or delirium preceding sudden death at times, or in other cases death occurring several hours to several days subsequent to exposure. In extreme concentrations, asphyxiation with death results from respiratory paralysis. When taken by mouth, the usual local signs and symptoms of an acute toxic gastritis are seen in addition to the general systemic manifestations. In treatment of acute benzol poisoning the patient should, of course, be removed from the danger area and placed in a comfortable reclining position. If carbon dioxide, oxygen, and respirator are at hand, this means of respiratory stimulation should be at once applied. If only oxygen tank and respirator be available, they may be used; and if no such apparatus be available, artificial respiration by the prone pressure or Schaeffer method should be applied until the patient has been breathing in a satisfactory manner for some minutes. The patient should be carefully watched, and at the first sign of respiratory failure or slowing of respiration the artificial respiration should be resumed. At all times it is important to keep the body warm by applying heat to the body and extremities. Cardiac and respiratory stimulants, such as caffein, may be given. In cases where benzol has been taken by mouth, the usual gastric lavage may be resorted to, followed by demulcents or bland drinks. Lecithin emulsion may be administered intravenously, as advocated by Nick, in doses of 5 cc. of a 10 per cent solution. Prolonged convalescence is essential in order to avoid complications.

Benzol Poisoning as an Industrial Hazard.—GREENBURG (*Public Health Reports*, 1926, **41**, 1410) *Chronic benzol poisoning:* The literature is reviewed and symptoms and treatment summarized as follows: Chronic benzol poisoning occurs with greater frequency in cold weather or the winter months when natural ventilation is usually reduced to a minimum by closed windows and doors so that the concentration of the poison in the atmosphere reaches a maximum. Atmospheric conditions of temperature and humidity also play an important part. At times of high heat and high humidity, other things being equal, spontaneous and sporadic outbreaks are most likely to appear. Young girls are especially predisposed to benzol poisoning, as are also pregnant women. Conditions of general ill health, tuberculosis, chlorosis, and other conditions lowering the general vitality or interfering with free function of the eliminative organs have a strong predisposing effect. The early symptoms comprise headache, dizziness, malaise, loss of appetite, ready fatigue, shortness of breath, and burning of the eyes, throat, and respiratory membranes. Later, nausea and vomiting, with epigastric burning and pain, may appear, and sensations of chilliness and general weakness, with bleeding from the mucous membranes of the nose, mouth, gastrointestinal tract, and genitourinary tract. Too frequent menstruation, with prolonged and uncontrollable bleeding from the vagina, is very common. About this time petechiæ and purpuric hemorrhages may appear on the body and extremities. Burnet regards purpura as a more serious prognostic sign than bleeding from the membranes. Other lesions of the skin may appear in the form of itching erythema, dry scaling, or vesicular papules. Later, complications affecting the central and peripheral nervous system may develop. Various forms of neuritis, with lesions affecting the dorsal column and the pyramidal tracts, may appear, giving rise to paresthesias, anesthesias, impaired locomotion, tremor, and trophic disturbances. The blood changes are typical. A leucopenia develops in most cases after exposure and increases in severity, although in some cases this is not absolute. The leucopenia may be extreme, reaching almost a complete absence of white blood cells. A reduction in the red-cell count then appears, but somewhat later than the leucopenia. The resultant anemia may become extreme, the red-cell count being lowered to less than 500,000 per c.mm. A corresponding reduction in the hemoglobin occurs to as low as 15 per cent. A considerable reduction in the platelet count appears, especially in the later stages of poisoning. Blood smears present the picture of an aplastic anemia showing but slight changes in the appearance of the red cells. Some pallor and anisocytosis are common. Almost complete absence of regenerative forms with very few megaloblasts and normoblasts are noted, with scantiness of platelets. A marked diminution of the granular types of white blood cells is seen, with a relative increase in the mononuclear forms. The leucotoxic effect is first noticed and is more pronounced on the myelocytic than on the lymphatic elements, so that an inversion of the leukocyte formula results. This gives a relative increase in the lymphocytes and a lowering of the polymorphonuclear forms. In rapidly developing cases, however, this inversion of the leukocyte formula may not appear, according to Fontana. A relative increase in the large mononuclear cells is common. Eosinophilia has also been noted in early poisoning, but this disappears rapidly on

cessation of exposure. The urine may show albumin, fat, casts, hemoglobin, and conjugated sulphur bodies. On autopsy the typical findings consist of hemorrhages in the skin, mucous and serous surfaces, and the viscera, pallor of the organs, with muscles of a deep-red color. Submucous hemorrhages are found along the gastrointestinal tract, in the pleura, pericardium and endocardium. The marrow of the long bones presents the typical picture of an aplastic anemia. The treatment in chronic benzol poisoning consists of change of employment in the very early cases, preferably to open-air work, together with the observance of general hygienic measures. These early cases generally respond very promptly to treatment. In the severe cases of advanced poisoning in which hemorrhages and anemia have occurred, treatment consists of rest, fresh air, sunshine, iron-containing foods, and the general hygienic measures that are used in combating secondary anemias, tonics, hydrotherapy, ultraviolet ray, etc. In advanced anemia with purpura and hemorrhages, McClure emphasizes the value of frequent and repeated blood transfusions. It is well to bear in mind that the anemia and other signs frequently continue and progress for long periods after removal from exposure, so that carefully adjusted treatment and prolonged convalescence are essential. The hazard is found in the following industries: chemical, rubber, celluloid, leather, cloth, Japanned goods, gas by-products, paints, varnishes, and others less important.

Endemic Goiter and Intelligence.—OLESON and FERNALD (*Public Health Reports*, 1926, **41**, 971) made their observations on 3796 sixth-grade school children in the Cincinnati public schools for the purpose of determining the effect, if any, of endemic goiter upon intelligence. Some degree of enlargement was found in about 25 per cent of the boys and in about 40 per cent of the girls, but the studies revealed no significant difference between thyroid-normal and thyroid-enlarged children. Children with marked enlargement seemed slightly less intelligent than the normal ones but the number in the group with marked enlargement was small.

A Note on an Experimental Pellagra-like Condition in the Albino Rat.—GOLDBERGER and LILLIE (*Public Health Reports*, 1926, **41**, 1025) have produced in the albino rat a syndrome which is analogous to pellagra in man. There is arrest of growth, loss of fur, ophthalmia, a dermatitis on the ears, neck, chest and legs; this is bilaterally symmetrical. In some cases there is fissuring or ulceration at the angles of the mouth. The condition is brought about by feeding a diet lacking in what appears to be a specific pellagra-preventing element, possibly in the nature of a vitamin.

Studies on the Etiology of Epidemic Encephalitis. I. The Streptococcus.—EVANS and FREEMAN (*Public Health Reports*, 1926, **41**, 1095) have confirmed the work of various European and American observers in isolating a streptococcus which seems to be the cause, or at least to be closely related to, epidemic encephalitis. The work is based on a single case, two others having proven negative. Symptoms are produced in animals (rabbits and monkeys) that are suggestive of the disease seen in human beings.

Results of Dick Tests Made on Different Groups.—DYER, CATON and SOCKRIDER (*Public Health Reports*, 1926, **41**, 1159) summarize their results as follows: Dick tests made on rural and suburban school children and children in city institutions gave a higher percentage of positive reactions among the rural and suburban groups. A relatively greater immunity was found to exist in males than in females, and this difference was found to increase with age. When two or more children from one family were tested there was a tendency for the reactions on the different children to agree. When disagreement occurred, the younger children were more often positive and the older children more often negative although the reverse was not rare. Differences in reactions caused by toxins produced by different streptococci of scarlatinal origin are noted, with the suggestion that different strains of scarlet fever streptococci may produce different toxins.

Clinical Observations on Endemic Typhus (Brill's Disease) in Southern United States.—MAXCY (*Public Health Reports*, 1926, **41**, 1213) calls attention to the frequency of typhus, 209 cases having been reported in Alabama and Georgia during the past three years. While the clinical picture varies very much the following gives the salient points: Onset is usually abrupt, with chills, fever, malaise, headache and prostration; in about one-third of the cases there are prodromal symptoms over several days. The temperature rises gradually, reaching its maximum between the fifth and eighth days. The second week sees a gradual decline and the fever is gone by the fourteenth day. A striking feature is the regularity of the duration of temperature, about fourteen days. In about three-fourths of the cases there is an eruption which appears oftenest on the fifth day, rarely as early as the second, and in 90 per cent before the eighth day. The evolution is rapid, becoming generalized within twenty-four hours of onset. It remains limited to mild cases, so far as distribution is concerned. Usually the palms and soles were spared. The color is dark red to red with a purple tinge. It disappears in from forty-eight to seventy-two hours. The spots are irregular in size, color, duration, elevation, outline and distribution. In only 6 of 114 cases studied did it appear to be absent. Respiratory symptoms were usually limited to a short, hacking cough. Two cases developed bronchopneumonia. Usually nausea accompanies the onset, sometimes with vomiting. Constipation was the rule; the abdomen flat and scaphoid. In only a small proportion of the cases was the spleen palpable. Some headache accompanied the onset and pain in the back was common. Muscular aching was complained of. Patients were dull or apathetic and sometimes delirious, or a condition of nervousness existed. Convalescence was slow; a month or two elapsed before work was resumed. Complications were rare—2 cases of bronchopneumonia, 1 of femoral thrombosis and 1 of suppurative parotitis. The death rate is probably from 2 to 4 per cent. On the laboratory side there are observed either marked leukopenia or marked leukocytosis. The Felix-Weil reaction was positive in the great majority of cases. The suggestion is made that, while clinically and serologically the disease is indistinguishable from mild typhus the epidemiology is not characteristic, and the mode of transmission may be different.

Tularemia: Hereditary Transmission, Infection by the Wood Tick, Dermacentor Andersoni Stiles.—PARKER and SPENCER (*Public Health Reports*, 1926, **41**, 1403) in an earlier report had demonstrated that Bacterium tularense (the cause of tularemia) was transmitted from the larvæ to adult of the wood tick (Dermacentor andersoni Stiles). In the present report is shown the hereditary transmission from infected adult female ticks to their progeny, the organism being demonstrated in ova, larvæ, nymphs, originating with infected females. This appears to be the first example of hereditary transmission, in insects, of a bacterium, though such transmission is known for certain protozoa.

The Susceptibility of the Coyote (Canis Lestes) to Tularemia.—PARKER and FRANCIS (*Public Health Reports*, 1926, **41**, 1407) report that a case came under observation in which a man appeared to have acquired tularemia from the bite of a coyote. This opened the question as to whether the coyote was himself infected or whether he served merely as a vector of organisms from an infected rabbit. Feeding experiments succeeded in conveying the infection to coyotes which died of acute tularemia, verified by serologic and animal tests.

Intradermal Smallpox Vaccination.—FORCE (*U. S. Pub. Health Rep.*, 1927, **42**, 1031) quotes the early students of vaccination and inoculation to show that they recognized what are now called "reactions of immunity" and the administrative fields of use for these reactions is discussed. A modification of the usual methods of evaluating the reactions following vaccination is described. Briefly, this consists of the intradermal injection of a measured volume of a given dilution of vaccine virus and the reading of the results. A heated control is always employed. The method is suggested for cases in which the cutaneous test fails to give satisfactory reactions.

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